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ABSTRACTS OF WORLD MEDICINE

It is the aim of this journal to provide the reader with abstracts of all important articles appearing in medical periodicals published in every part of the world, and in this way to enable him to keep in touch with new developments throughout the whole field of medicine and in each of its special branches, including those aspects of surgery which are of particular concern to the physician.

More than 1,600 periodicals are surveyed, from which are selected for abstracting those papers which appear to make some useful contribution to the sum of medical knowledge or experience. Each paper is abstracted in sufficient detail to indicate to the general reader the nature and value of that contribution and to enable the specialist to assess its importance in relation to his own work and to decide whether the original article should be read in full. The author's own summary or an editorial summary published with the original article may occasionally be reproduced if it is suitable for these purposes, and the title and reference alone may be published in order to draw attention to a review article or other type of paper which cannot readily be abstracted.

The abstracts in each issue are grouped in sections according to subject and, so far as possible, those dealing with medical and surgical aspects of the same problem appear together. The titles of papers written in languages other than English are given both in translation and in the original form. The titles of journals are given in full and also abbreviated according to the rules adopted in the *World List of Scientific Periodicals*, as modified by *ISO Recommendation R4: International Code for the Abbreviation of Titles of Periodicals* (International Standards Organization, 1957), and in *World Medical Periodicals* (Second Edition, World Medical Association, 1957). The transliteration of authors' names from the Cyrillic alphabets is in accordance with *ISO Recommendation R9: International System for the Transliteration of Cyrillic Characters* (International Standards Organization, 1955).

Explanatory or critical comments by the abstracter or editor are enclosed within square brackets.

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Pathology

EXPERIMENTAL PATHOLOGY

559. **Incomplete Carcinogens in Cigarette Smoke Condensate: Tumour-promotion by a Phenolic Fraction**
F. J. C. ROE, M. H. SALAMAN, and J. COHEN. *British Journal of Cancer* [*Brit. J. Cancer*] **13**, 623–633, Dec., 1959 [received Feb., 1960]. 2 figs., 31 refs.

In a number of experiments carried out in the Cancer Research Department, London Hospital Medical School, the authors examined tobacco-smoke condensate for incomplete carcinogens. After mice of the " 101 " inbred strain had been treated with dimethylbenzanthracene a phenolic fraction of cigarette-smoke condensate was found to have a strong tumour-promoting action. The same dose of dimethylbenzanthracene alone produced only a few tumours and the phenolic fraction alone produced none. Whole-smoke condensate or the neutral fraction of the condensate caused a few papillomata only. It is suggested that cigarette smoke is richer in tumour-promoting than in tumour-initiating activity, such activity probably being in the phenolic compounds.

G. Calcutt

560. **Blood Pepsinogen and Gastric Erosions in the Rat**
R. ADER, C. C. BEELS, and R. TATUM. *Psychosomatic Medicine* [*Psychosom. Med.*] **22**, 1–12, Jan.–Feb., 1960. 5 figs., 13 refs.

The relationship between blood pepsinogen levels and the occurrence of gastric erosions in the rat was studied at the University of Rochester Medical Center, Rochester, New York. The susceptibility of different strains of rat to gastric erosion and the differential susceptibility of male and female rats were also studied. Three separate experiments were conducted and in each the rats were subjected to a standard immobilization procedure and deprived of food and water for 20 hours. The blood pepsinogen level was determined from a 1-ml. sample of plasma. Gastric erosions observed post mortem were examined macroscopically and microscopically.

In the initial experiment there proved to be a higher incidence of gastric erosions in Wistar than in Sprague–Dawley or Long–Evans rats. In another experiment half of each strain served for experimental and half for control purposes. None of the controls developed gastric erosion, but 7 out of 36 male and 32 out of 42 female experimental animals had from 1 to 18 gastric erosions. No strain differences were apparent in the males, but female Wistar rats had more erosions per animal than did Sprague–Dawley females. Finally, significantly higher pepsinogen levels were found in both male and female experimental animals with gastric erosions than in those without erosions. High pepsinogen levels were also found occasionally in control animals without erosions.

It is concluded that a raised plasma pepsinogen concentration reflects susceptibility to, rather than the presence of, gastric erosion.

A. Balfour Sclare

561. **The Pathologic Effects of Intravenously Administered Soluble Antigen–Antibody Complexes. I. Passive Serum Sickness in Mice**
R. T. MCCLUSKEY, B. BENACERRAF, J. L. POTTER, and F. MILLER. *Journal of Experimental Medicine* [*J. exp. Med.*] **111**, 181–194, Feb. 1, 1960. 8 figs., 25 refs.

The authors, working at New York University–Bellevue Medical Center, have produced in mice renal, arterial, and endocardial lesions characteristic of serum sickness by the intravenous injection of soluble antigen–antibody complexes, these being prepared by forming immune precipitates at equivalence and dissolving the precipitate in excess antigen. The mice were given intravenous injections of complexes containing 3 mg. of antibody protein.

It was shown that rabbit antibovine serum albumin, rabbit antiovalbumin, and chicken antibovine serum albumin complexes were effective. Only the rabbit systems caused acute anaphylactic shock; the administration of the antihistamine " phenergan " (promethazine hydrochloride) prevented death from anaphylaxis, though it had no effect on the renal lesions. In 49 out of 55 mice the rabbit antibovine serum albumin complex caused glomerulonephritis, which was characterized by enlargement and hypercellularity of the glomeruli, with swelling of the endothelial cells and neutrophil granulocyte infiltration. Focal necrosis of the small muscular arteries occurred in 6 animals and endocarditis in 3. Unlike the lesions in Masugi's nephritis, however, these changes were self-limiting and even after 6 injections over a period of 3 days complete histological recovery occurred within a month. Cortisone diminished but did not abolish the nephritis, while it increased the amount of amorphous eosinophilic material seen in the glomerular capillary loops. The authors regard this material as an immune precipitate and suggest that its increase was due to the inhibitory effect of cortisone on

the uptake of the immune complexes by the reticulo-endothelial system and the paucity of neutrophils in the glomeruli.

The inability of the soluble complexes to sensitize guinea-pig skin in the passive cutaneous anaphylaxis reaction suggested that the complexes do not dissociate appreciably *in vivo*. In view of the observations that the chicken complexes did not cause anaphylaxis and that chicken antibody fixed little complement in the presence of its antigen, in contrast with the ability of the chicken complexes to produce glomerulonephritis, the authors suggest that the liberation of vasoactive amines, which occurs in anaphylaxis, is not essential for the production of nephritis and they consider that complement plays only a small role. From the over-all results they conclude that the tissue changes, which were maximum within 4 days of injection, were a direct response to the injected complex and not due to an immunological reaction by the recipient; they suggest that the localization of the lesions was determined by the localization of the soluble complexes, which was similar to that of other injected colloids. *G. L. Asherson*

562. **The Pathologic Effects of Intravenously Administered Soluble Antigen–Antibody Complexes. II. Acute Glomerulonephritis in Rats**

B. Benacerraf, J. L. Potter, R. T. McCluskey, and F. Miller. *Journal of Experimental Medicine* [*J. exp. Med.*] **111**, 195–200, Feb. 1, 1960. 5 figs., 6 refs.

In the second part of this study [see Abstract 561] acute glomerulonephritis was produced in rats by the intravenous injection of soluble antigen–antibody complexes, the condition appearing in 13 out of 15 animals given an injection of 30 to 60 mg. of antibody protein in the form of a soluble complex over a period of 24 hours. Both bovine serum albumin–rabbit antibovine serum albumin and ovalbumin–rabbit antiovalbumin complexes were effective. As in mice the nephritis was characterized by enlarged, hypercellular glomeruli with swollen endothelial cells and slight neutrophil granulocyte infiltration; in contrast to the results in mice, however, no lesions were seen in the heart, lung, liver, or spleen. Proteinuria and urinary loss of bovine serum albumin occurred in the rats given the bovine serum albumin complex, 2 out of 15 animals showing casts and erythrocytes and leucocytes in the urine. The blood urea nitrogen level was raised in all of 10 animals in which it was determined, the highest value being 87 mg. per 100 ml. No changes were found in the animals receiving bovine serum albumin alone.

The authors contrast these changes with the reported severe renal damage caused in rats by the injection of potent anti-kidney serum (Masugi nephritis), such animals developing the nephrotic syndrome and often dying in uraemia. In that instance the basement membrane was the primary site of involvement, whereas in the glomerulonephritis produced by the present soluble complexes the glomerular endothelial cells were primarily involved, the basement membrane being unaffected. Also the nephritic lesions resolved completely after the injections were discontinued. *G. L. Asherson*

CHEMICAL PATHOLOGY

563. **The Measurement of Folic Acid Activity in Serum: a Diagnostic Aid in the Differentiation of the Megaloblastic Anemias**

V. Herbert, H. Baker, O. Frank, I. Pasher, H. Sobotka, and L. R. Wasserman. *Blood* [*Blood*] **15**, 228–235, Feb., 1960. 23 refs.

In this study from the Mount Sinai Hospital, New York, a method is described by which the folic acid activity of fasting serum may be determined. The technique is microbiological, *Lactobacillus casei*, which utilizes "folic-acid-active" materials for its growth, being the organism used. The results in 10 normal subjects were 7·5 to 24 mμg. per ml. In 6 cases of refractory non-megaloblastic anaemia of unknown cause, one case of megaloblastic anaemia in an Indian who abstained from all forms of animal protein on religious grounds, 10 cases of pernicious anaemia, and one of megaloblastic anaemia following ileal resection they were within the normal range. In 3 cases of nutritional megaloblastic anaemia, 3 of megaloblastic anaemia associated with alcoholic cirrhosis, 2 of megaloblastic anaemia in infancy, 2 of the same condition in pregnancy, and 7 of megaloblastic anaemia associated with the malabsorption syndrome all values were below 5 mμg. per ml. In 9 further instances unidentified sera were supplied from other hospitals and the results correlated with the clinical diagnoses subsequently made. In 5 of these sera the level of folic acid activity was low and these proved to be from patients with folic acid deficiency; the other 4, in which the level was normal, came from patients with vitamin-B_{12} (cyanocobalamin) deficiency.

[The segregation of megaloblastic anaemias due to vitamin-B_{12} deficiency from those caused by folic acid deficiency has been greatly aided by the availability of microbiological assays for vitamin B_{12} in serum. That such a diagnostic aid should now be available for the diagnosis of folic acid deficiency will be of great value in the assessment of megaloblastic anaemia.]

H. Lehmann

564. **An Evaluation of Serum Transaminase in the Jaundice States**

H. J. Sacks and G. F. Lanchantin. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] 33, 97–108, Feb., 1960. 6 figs., 34 refs.

The use of the determination of serum glutamic oxalacetic transaminase (SGOT) in 120 patients with jaundice of varying etiology is described. Values for SGOT of 1,000 units and more were observed to be diagnostic of hepatocellular damage. Values exceeding 500 units of SGOT per ml. seem to exclude presumptively surgical obstructive jaundice, and such values were observed in most instances of viral hepatitis, hepatitis associated with "marsalid" (iproniazid), and in massive hepatic necrosis. The levels in 3 patients with carcinoma of the liver and 3 with pancreatitis also exceeded this amount. Values less than 500 units of SGOT per ml. were nonspecific for the type of jaundice present. In this range, SGOT:bilirubin ratios greater than 40 pre-

sumptively exclude duct-obstruction; ratios less than 40 presumptively exclude hepatitis. In the presence of jaundice and levels for SGOT in excess of 500 units, data on serum glutamic pyruvic transaminase (SGPT) do not provide additional information. With values for SGOT less than 500 units SGPT may be of help in excluding hepatitis from consideration if the SGOT: SGPT ratio exceeds 3·18. On the other hand, the ratio is not suitable for distinguishing duct-obstruction from cirrhosis.—[Authors' summary.]

565. **Ascorbic Acid Inhibition of the Glucose-oxidase Test for Glycosuria**
P. O'GORMAN, P. D. GRIFFITHS, and H. R. BLOXAM. *British Medical Journal* [*Brit. med. J.*] **1**, 603–606, Feb. 27, 1960. 3 figs., 10 refs.

At Guy's Hospital, London, a false negative reaction to the glucose oxidase paper test was obtained during a glucose tolerance test in a diabetic patient receiving ascorbic acid therapeutically. This observation led the authors to study the extent of inhibition of the glucose oxidase paper reaction to varying amounts of glucose at varying concentrations of ascorbic acid. In view of their findings, which are shown graphically, they then studied the urinary excretion of ascorbic acid in healthy adults. After administration of 300 mg. of ascorbic acid daily for 7 days to 22 healthy volunteers a random specimen of urine was collected from each. It was found that 11 of the 22 specimens contained sufficient ascorbic acid to prevent the detection by the glucose oxidase paper test of at least 500 mg. of glucose per 100 ml. This amount of glucose is easily detectable by Benedict's test. It is suggested that since ascorbic acid is likely to be an important cause of false negative results, the glucose oxidase paper test should be used in intelligent conjunction with Benedict's test and paper chromatography.

M. Sandler

566. **The Diagnosis of Porphyria by Means of Biochemical Laboratory Tests.** (Laboratorní postup při diagnóze porfyrické choroby)
J. BERMAN. *Časopis lékařů ceských* [*Čas. Lék. čes.*] **99**, 193–197, Feb. 19, 1960. 6 figs., 13 refs.

In Czechoslovakia 140 cases of porphyria have been reported so far, of which 21 were cases of porphyria cutanea tarda, while none were of the acute or mixed type. An exact diagnosis depends on biochemical examinations, the results of which are always positive in acute cases, but may be negative in the latent forms of porphyria. The present author lists 9 such tests—stereoscopic examination of the urine, examination of the urine under ultraviolet light, examination of the urine by the talcum test for porphyrins, by specific tests for coproporphyrin and uroporphyrin, and by the Ehrlich aldehyde test for porphobilinogen, examination of duodenal juice and faeces for porphyrins, and puncture biopsy of the liver.

Of these, he recommends the talcum test and Ehrlich's aldehyde test for routine use in biochemical laboratories to avoid the danger of failure to diagnose porphyria, which very often remains latent for shorter or longer periods. By the application of the other tests listed it is possible to differentiate the various types of porphyria, while as additional aids the author mentions the quantitative determination of the porphyrins and porphobilinogen in porphyric urine and the crystallization of porphyrins for the preparation of standard solutions and the determination of the melting point. *M. Hrusak*

HAEMATOLOGY

567. **The Macrocytosis of Hepatic Disease. II. Thick Macrocytosis**
J. BINGHAM. *Blood* [*Blood*] **15**, 244–254, Feb., 1960. 2 figs., 8 refs.

In a previous paper from the University of Toronto (*Blood*, 1959, **14**, 694; *Abstr. Wld Med.*, 1960, **27**, 83) the author reported that in a study of 222 patients suffering from a variety of hepatic diseases it was found that no less than 137 (62%) had a macrocytic blood picture. Three types could be distinguished: (1) thin macrocytosis, present in 81 cases, in which all the macrocytes were flattened so that the diameter was increased but the volume remained unchanged; (2) target macrocytosis, present in 39 cases, in which a proportion of the thin macrocytes had become target cells; and (3) thick macrocytosis, present in 17 cases, in which, in addition to thin macrocytes, thick macrocytes were present in sufficient numbers to raise the mean corpuscular volume to 110 c.μ or more. Thin macrocytosis having been discussed in the first paper, the present article deals with thick macrocytosis. All of the 17 patients in this group had free hydrochloric acid in the gastric juice. On examination of the bone marrow 6 showed macronormoblastic, 4 atypical megaloblastic, and 5 frank megaloblastic maturation. Of the 17 patients, 15 suffered from Laennec's cirrhosis and 2 from post-necrotic cirrhosis. In the peripheral blood picture the anisocytosis was much more pronounced in liver disease than in pernicious anaemia.

The author considers the cause of thick macrocytosis to be a dietary factor, since the disorder developed only in patients in whom hepatic disease was accompanied by dietary deficiency. He suggests that while disease of the hepatic parenchymal cells is generally associated with the macronormoblastic type of erythrocyte maturation, which results in thin macrocytosis, when severe protein malnutrition is superadded atypical and genuine megaloblasts arise in the bone marrow, causing thick macrocytosis. *H. Lehmann*

568. **A Hitherto Undescribed Phenomenon in ABO Haemolytic Disease of the Newborn**
S. LEWI and T. K. CLARKE. *Lancet* [*Lancet*] **1**, 456–458, Feb. 27, 1960. 1 fig., 7 refs.

In this article from the National Blood Transfusion Centre, Paris, the authors refer to the inadequacy of laboratory tests in the diagnosis of ABO haemolytic disease of the newborn and report some interesting observations on the sedimentation of erythrocytes from the cord blood of affected infants. Heparinized samples

of cord blood were centrifuged and the cells washed three times in buffered isotonic saline, packed, and made up as a 25% suspension in a special polyvinylpyrrolidone (P.V.P.) medium. The mixtures were allowed to sediment in Westergren tubes and readings were taken at 5-minute intervals. The authors describe their method of controlling each batch of P.V.P. medium to give a standard sedimentation rate of 5 mm. in 10 minutes with the cord-blood erythrocytes of normal, full-term, ABO-compatible infants, and state that the medium remains stable for a considerable time.

Of 3,924 cord-blood samples tested, 835 were incompatible in the ABO system with the mother's blood. (Children with Rh haemolytic disease, stillbirths, and those not observed for at least 3 days after birth were excluded.) In all compatible samples the rate of sedimentation was 5 mm. in 10 minutes, sedimentation continuing at a rate of 5 mm. every 5 minutes. Incompatible samples showed a wide range of variation and were classified into 3 groups: (1) with greatly accelerated sedimentation (90 mm. or more in 10 minutes); (2) with moderately accelerated sedimentation, clear delineation between packed and suspended cells being absent during the first 10 to 15 minutes; and (3) with normal or slightly accelerated sedimentation. Eight samples fell into Group 1; the infants from whom they were taken all had severe haemolytic disease, details of which are given. In Group 2 there were 25 infants, none of whom were anaemic, but 17 of whom were severely jaundiced. In Group 3 the incidence of jaundice was no greater than in the control group of ABO-compatible infants.

The authors briefly discuss some of the difficulties in the serological diagnosis of ABO haemolytic disease and stress that the increased rate of cord-blood erythrocyte sedimentation observed by them does not occur in Rh haemolytic disease..

[This article should be read in the orginal by those interested in the subject.] *E. G. Hall*

569. **The Significant Percentage of Blast Cells in the Bone Marrow in the Diagnosis of Acute Leukaemia**
J. W. Ibbott, D. M. Whitelaw, and J. W. Thomas. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **82**, 358–361, Feb. 13, 1960. 17 refs.

Difficulty is sometimes experienced in distinguishing acute leukaemia from leukaemoid reactions due to a variety of conditions, particularly in children. The problem therefore arises of determining the lowest percentage of blast cells which can be regarded as diagnostic of acute leukaemia. An analysis was made of the results of 1,827 consecutive bone-marrow examinations carried out during the 5-year period 1953–57 in the Department of Haematology, Vancouver General Hospital. A blast-cell count greater than 6% was found in 129 cases and 127 of these were confirmed cases of acute leukaemia. In the remaining 2 cases, in infants aged 4 weeks and 5 months, the diagnosis was an allergic leukaemoid reaction and megaloblastic anaemia of infancy respectively. In a further 48 cases the blast-cell count was between 2% and 6% and in 6 of these there was acute leukaemia in remission or in an early stage of development. A large variety of benign haematological disorders were present in the remaining 42 cases. The authors state that marrow blast-cell counts up to 2% are not significant, since such counts are not infrequently observed in the marrow of healthy individuals. *A. W. H. Foxell*

MORBID ANATOMY AND CYTOLOGY

570. **The Histochemistry of the Hormone-active Tumours of the Adrenal Cortex.** (Гистохимия гормональноактивных опухолей коры надпочечника)
E. I. Tarakanov and T. A. Ščitkova. *Проблемы Эндокринологии и Гормонотерапии* [*Probl. Endokr. Gormonoter.*] **6**, 68–74, Jan.–Feb., 1960. 8 figs., 23 refs.

Basing their conclusions upon the histological study of 5 hormone-active tumours of the adrenal cortex the authors divide such tumours into two types: (1) corticosteromata consisting of light-coloured cells filled with lipids, and (2) androsteromata formed of dark cells containing only a little lipid but much ketosteroid; in one of the authors' cases the tumour was mixed, consisting of both the above elements. The corticosteroma produces the " Itsenko–Cushing " syndrome, while the androsteroma causes virilism and hirsutism and may be malignant, as in one of the present cases. Sections were set aside for biosynthesis experiments with various substrates, chiefly progesterone, while other histological sections were variously stained to show the general structure of the tumour, its content of fats and lipids (scarlet red), ascorbic acid (method of Girou and Leblon), cholesterol (Schultz), ketosteroids (Ashbel and Seligman), and ribonucleic acid (Brachet).

In the case of the corticosteromata the products of biosynthesis were not different qualitatively from those of hyperplastic adrenal glands, whereas those obtained from the androsteromata included 17-α-oxyprogesterone; however, in the one malignant tumour in the series the normal biosynthesis was disturbed and 17-oxycorticosterone and corticosterone were not synthesized, while progesterone was converted into a sexually inert substance believed to be δ-1:4-androstadien-17-β-ol-3-one. The tumour content of ribonucleic acid, glycoproteins, and ascorbic acid was found to be much greater in the androsteromata than in the corticosteromata. There are grounds for concluding that nucleoli and nuclear structures generally take an active part in the synthesis of steroid hormones. *L. Firman-Edwards*

571. **The Pathology of Neonatal Hepatitis**
B. Ruebner. *American Journal of Pathology* [*Amer. J. Path.*] **36**, 151–163, Feb., 1960. 10 figs., 23 refs.

In this paper from the Department of Pathology, Dalhousie University, and the Pathology Institute of Nova Scotia, Halifax, Canada, the author discusses the histological appearances of the liver in 4 cases of neonatal hepatitis and 4 of extrahepatic biliary atresia. Of the 4 infants with hepatitis, 3 died from liver failure between the ages of 6 weeks and 3 months; liver tissue for examination was obtained at necropsy. In the remaining patient, who survived, liver biopsy was performed at

the age of 2½ months. Surgical biopsy specimens were obtained from 3 of the infants, aged 3 to 18 months, with biliary atresia, and necropsy material from one who died at the age of 15 months. In the patients with hepatitis dissection and injection of indian ink at necropsy or cholangiography at operation showed that the biliary tree was patent. In the 3 cases of atresia in which necropsy was not performed the condition was diagnosed at laparotomy.

The author describes a total of 17 histological abnormalities observed in the liver sections, including the presence of giant cells, degenerative and inflammatory changes, bile-duct proliferation, bile stasis, fibrosis, haematopoietic foci, and haemosiderin, and grades the severity of these in each case. Although there were differences between the two groups in the number of giant cells present, the degree of proliferation of intralobular bile ductules and perilobular bile ducts, the distribution of inflammatory and fibrotic changes, and the number of haematopoietic foci, there was some overlap and considerable variation within each group. Discussing these abnormalities with reference to the findings of other workers he suggests that in some cases of hepatitis there may be a marked perilobular duct proliferation analogous to "cholangiolitic" hepatitis in adults. He considers that the presence of injected indian ink in the bile canaliculi does not support the view that the hepatitis lesion is due to maldevelopment of the intrahepatic biliary system.

[The histological problem of distinguishing between neonatal hepatitis and atresia usually resolves itself into a study of liver biopsy material obtained before the age of 3 months. The author's material is not entirely appropriate as a basis of comparison for this purpose.]

E. G. Hall

572. **Testicular Lesions of Periarteritis Nodosa, with Special Reference to Diagnosis**

E. V. DAHL, A. H. BAGGENSTOSS, and J. H. DEWEERD. *American Journal of Medicine* [*Amer. J. Med.*] **28**, 222–228, Feb., 1960. 4 figs., 13 refs.

In this study, undertaken at the Mayo Clinic to determine the value of testicular biopsy examination in the diagnosis of periarteritis nodosa, the authors have examined the records and histological sections of formalin-fixed blocks of the testes of 44 patients aged 11 to 71 (average 47) years seen at the Clinic during the period 1931–55, in 30 of whom the diagnosis of periarteritis nodosa was established or suspected. Abnormalities suggestive of the disease were found in 41 (93%) of these cases. Diagnostic arterial lesions were seen in 38 cases (86%), while less common changes included infarcts, degeneration or disappearance of the tubules, haemorrhage, and haematoma. Clinical abnormalities of the testis had been observed in only 8 of the patients (18%), though the size had been recorded as subnormal in 11 (25%).

By sampling different sectors of the histological sections the authors made a rough estimate that positive diagnostic signs of periarteritis in a single testicular biopsy specimen could be expected in only about 1 in 5 male patients (22%). Testicular biopsy in the living patient is therefore recommended only when clinical findings suggestive of periarteritis are accompanied by testicular abnormalities and there are, moreover, no detectable cutaneous, subcutaneous, or muscular lesions. If biopsy is performed the specimen should include part of the tunica vasculosa as well as some of the underlying parenchyma.

A. Wynn Williams

573. **The Muscular Lesions of Familial Periodic Paralysis.** (Les lésions musculaires de la paralysie périodique familiale)

J. E. GRUNER and A. PORTE. *Revue neurologique* [*Rev. neurol.*] **101**, 501–523, Oct., 1959 [received Feb., 1960]. 22 figs., 27 refs.

The authors present from the Faculty of Medicine, Strasbourg, a review of familial periodic paralysis, together with an account of a family showing disease of this type which was present in five generations and was inherited as a dominant characteristic. The condition was characterized clinically by sudden episodes of paralysis and by muscular hypertrophy and myotonia. The motor disturbances and electrical abnormalities persisted between the acute episodes of paralysis and became more pronounced as time went on.

Muscle biopsies were performed in 3 cases, part of the specimen being used for routine histological examination, while the remainder was fixed in Palade's osmic acid fixative and embedded in methacrylate for examination by electron microscopy. It was shown histologically that the lesions are characterized by hypertrophy of muscle fibres, central location of nuclei, disorganization of myofibrils, and degeneration of sarcoplasm. The change in sarcoplasm takes the form of focal areas of granular change, together with accumulation of glycoprotein material; extreme vacuolation of sarcoplasm can also occur. Electron microscopy demonstrated the presence of sarcoplasmic vesicles analagous to lysosomes and revealed lysis of myofibrils. The process sometimes amounts to a focal necrosis of muscle fibres. The lesions are regarded by the authors as differing from those of juvenile myopathy, Steinert's disease, ischaemia, and neurogenic atrophy; rather they resemble those which have been described in certain experimental myopathies related to disturbance of potassium metabolism or certain deficiency states.

H. A. Sissons

574. **The Incidence and Characteristics of Lewy Bodies in Idiopathic Paralysis Agitans (Parkinson's Disease)**

J. BETHLEM and W. A. DEN HARTOG JAGER. *Journal of Neurology, Neurosurgery and Psychiatry* [*J. Neurol. Neurosurg. Psychiat.*] **23**, 74–80, Feb., 1960. 7 figs., 22 refs.

At the Neurological Clinic, University of Amsterdam, the brains of 15 patients dying of idiopathic Parkinson's disease and of 4 who had the post-encephalitic form of the disease were exhaustively examined in an attempt to characterize the nature of Lewy inclusion bodies. Such bodies are found in the degenerated neurones of the substantia nigra, substantia innominata, and locus coeruleus in probably all cases of idiopathic Parkinsonism, but have very rarely been found either in the brains of

patients with the post-encephalitic form or in those of non-Parkinsonian patients. The authors showed histochemically that these inclusion bodies contain no lipids, polysaccharides, or nucleoproteins; further, no calcium, iron, fibrin, mucin, or glycogen could be detected, nor could the presence of heavy metals, which are themselves capable of producing intranuclear inclusions, be demonstrated by microradiography. They did show, however, that the core of these bodies consists of proteins containing aromatic α-amino-acids.

On the assumption that these bodies could conceivably be viral inclusions—although the staining reactions did not completely warrant such an assumption—a suspension of substantia nigra removed within 3 hours of death from 5 patients dying of idiopathic Parkinsonism was injected intracerebrally into a wide range of animals, including cynomolgous monkeys. No transfer of the lesion was obtained. The authors briefly comment upon the manner in which these findings agree with those of other workers, notably Greenfield and Bosanquet (*J. Neurol. Neurosurg. Psychiat.*, 1953, **16**, 213; *Abstr. Wld Med.*, 1954, **16**, 92). They point out the great theoretical significance of the finding of Lewy inclusion bodies in the substantia innominata in 9 of their 15 cases of idiopathic Parkinsonism, and suggest that a better understanding of the nature of these bodies may be the key to the pathogenesis of the disease. *J. B. Cavanagh*

575. **Incidence of Cerebral Infarction Associated with Ruptured Intracranial Aneurysms: a Study of 8 Unoperated Cases of Anterior Cerebral Aneurysm**
S. H. Birse and M. I. Tom. *Neurology* [*Neurology (Minneap.)*] **10**, 101–106, Feb., 1960. 10 figs., 2 refs.

The authors of this paper from the University and the General Hospital, Toronto, examined the brains of 8 patients who died following rupture of a berry aneurysm, the object being to determine the exact cause of death in such cases. None of the patients had been subjected to operation, and in all of them the aneurysm was situated on the anterior communicating or the anterior cerebral artery. Five of the aneurysms contained recent or agonal thrombi. In 7 cases there was extensive cerebral infarction in the area supplied by the affected vessel, and in 6 of these further infarctions in other vascular territories were demonstrated. [How these came about is not made clear.] The authors did not consider that thrombotic embolism was a likely cause, and in one case this could be safely excluded. *J. B. Cavanagh*

576. **Changes in the Brain Associated with Senility**
K. M. Wahal and H. E. Riggs. *A.M.A. Archives of Neurology* [*A.M.A. Arch. Neurol.*] **2**, 151–159, Feb., 1960. 7 figs., 22 refs.

At the Laboratory of Neuropathology, Philadelphia General Hospital, the authors have studied comparable areas of the brain of three groups of patients, as follows: (1) Fifteen patients, of whom 8 were over 80, who had died with senile intellectual deterioration without focal deficit or frank psychosis, but in whom varying degrees of lethargy, loss of memory and attention, irritability or depression, retardation of movement and speech, tremors, and shuffling gait had been present. In these patients episodes of cardiac insufficiency had occurred for 2 to 8 years. Hypertension, cardiac hypertrophy, extensive myocardial fibrosis or healed infarcts, and aortic atheroma of varying degree were found in some of the cases and all but one showed renal damage, while chronic pulmonary disease was present in 6 of the cases. (2) Twelve patients aged 30 to 55 dying of chronic heart disease in whom cardiac insufficiency had been present for one to 10 years; all of these showed cardiac hypertrophy and 8 exhibited minimal or mild degrees of aortic atheroma, while chronic renal damage was present in 6. (3) The third group consisted of 8 patients aged 18 months to 12 years with heart disease in whom cardiac insufficiency had been present for one or more years.

In the senile group surprisingly mild macroscopic changes, such as moderate widening and deepening of the cortical fissures, were observed. In 8 brains ventricular dilatation limited to the anterior horns of the lateral ventricles was present, while thickening and opacity of the leptomeninges over the vertex and convexity of the hemispheres occurred in more than half the specimens. Atheroma was present in the basal arteries in 10 brains, but in no instance did this impinge upon the lumen. Comparable degrees of convolutional atrophy were present in 2 of the brains of patients in Group 2 and in one from Group 3, while meningeal fibrosis occurred in 4 and 3 brains from these two groups respectively. A study of sections from the cerebral cortex, subcortical ganglia, brain stem, and cerebellum showed that in the senile brains cellular degeneration, lipofuchsin deposition in the neurones, and thickening and collagenization of the walls of the intracerebral vessels were severe and widespread. Essentially the same pattern of changes was seen in the cardiac cases of both age groups, differing only in the extent and intensity of the process. Alterations of cytoarchitecture were present throughout the neuraxis, but were most easily identified in the cerebral cortex and the inferior olivary and dentate nuclei. [For a detailed description of these changes the original paper and its photomicrographs should be consulted.]

It is concluded that senile mental changes may develop in the absence of focal infarcation or occlusive disease of the cerebral arteries. While atheromatous changes were prominent in the cerebral vessels in many of the cases, in others they were absent or slight. In the latter group of cases, however, repeated or prolonged episodes of cardiac decompensation were features of the clinical course of the disease. Other workers have ascribed the changes in the senile brain to arteriosclerosis. However, since equivalent brain damage was seen in some of the juvenile cardiac cases and since obstructive cerebral arterial disease was absent in some senile brains the authors conclude that cardiac insufficiency as well as local cerebral vascular disease may play a part in the causation of cellular degeneration in the brain in old age. In these circumstances disorders of systemic circulation may exert sufficient influence upon cerebral blood flow, even in the absence of stenosis of cerebral vessels, to result in neural dysfunction. *R. Wyburn-Mason*

Microbiology and Parasitology

577. **Value of Antirabies Vaccine With and Without Serum against Severe Challenges**
N. VEERARAGHAVAN and T. P. SUBRAHMANYAN. *Bulletin of the World Health Organization* [*Bull. Wld Hlth Org.*] **22**, 381–391, 1960.

Earlier studies with antirabies serum and vaccine have been extended to determine the value of serum, vaccine, or serum and vaccine combined against rabies challenges of increasing degrees of severity. While serum alone was not found to have any protective effect, vaccine alone was sufficient against mild challenges, the superiority of combined therapy with both serum and vaccine becoming evident at a challenge of about 50 LD_{50}. With challenges of over 300 LD_{50} no treatment was of any value. It was also found that with a recommended optimum dose of serum, the usual vaccine dose could be halved on a matter of importance in countries with a high incidence of neuroparalytic accidents following administration of nervous tissue vaccine.—[Authors' summary.]

578. **Flocculation Tests in Hydatid Disease**
A. FISCHMAN. *Journal of Clinical Pathology* [*J. clin. Path.*] **13**, 72–75, Jan., 1960. 14 refs.

The author of this paper from the Central Laboratory, Auckland Hospital, New Zealand, describes two new flocculation tests for the diagnosis of hydatid disease and compares the results with those obtained with the complement-fixation test. Polystyrene latex particles coated with hydatid cyst fluid were used in one of the flocculation tests and bentonite particles similarly coated in the other. These tests were found to be simpler to perform than the complement-fixation test and to be specific, 6·9% (of 102 sera) and 6·1% (of 126 sera) showing higher sensitivity in the latex and bentonite tests respectively than in the complement-fixation test. The latex test has the advantages that the preparation of sensitized particles is simpler and the result can be read with the naked eye. The bentonite test is more rapid, once the stock and sensitized particles have been prepared.

Using the latex test the author demonstrated antibody in the γ-globulin fraction of 3 positive sera. No antibody could be demonstrated in the γ-globulin fraction of 3 negative sera or in any other components of all 6 sera.
I. M. Rollo

579. **The Antigens of Various Helminths. Investigations by the Schultz–Dale Technique and Skin Tests in Man.** (À propos des antigènes de divers helmintes. Expériences de Schultz–Dale et tests cutanés sur l'homme)
R. BRUN and E. MUSSO. *Acta allergologica* [*Acta allerg.* (*Kbh.*)] **14**, 379–385, 1959. 2 figs., 6 refs.

At the University Dermatological Clinic, Geneva, the polysaccharide fraction of the antigens prepared from *Ascaris* from man, horse, and pig and also from *Taenia saginata* were studied for antigenic similarities, a scratch test and the Schultz–Dale technique being used. The results of skin tests showed that there was no cross-reaction in man between *Taenia* and *Ascaris*, but that there was a positive reaction to *Taenia* in carriers. With the Schultz–Dale technique the different worms were found to have one or several common antigens as well as a specific antigen for each species. *A. W. Frankland*

580. **Rapid Identification of Mycobacterial Colonies. I. The Auramine Test**
H. ERLICH. *American Review of Respiratory Diseases* [*Amer. Rev. resp. Dis.*] **81**, 218–225, Feb., 1960. 9 refs.

Working at the Arroyo Del Valle Sanatorium, Livermore, California, the author has devised a rapid test for identifying mycobacterial colonies. The basic reagent is a solution of 0·1 g. of auramine in 100 ml. of 95% ethyl alcohol which may be used in three different ways, as follows. (1) In the disk test disks of ½ inch (1·25 cm.) diameter cut from Whatman No. 1 chromatography paper are impregnated with auramine solution and dried. A small quantity of the suspected culture is then rubbed into the disk with a sterile applicator and 2 drops of an 0·5 N aqueous solution of sodium hydroxide are allowed to fall on to the disk. The author used a disk without auramine but with culture, and another disk with dye but without culture as controls. (2) In the auramine flood test 2 or 3 ml. of the same solution of auramine mixed with an equal volume of 1·0 N aqueous NaOH solution is poured over the culture growing at 37° C. on oleic-acid–albumen–agar medium. (3) The auramine fluorescence test, in which the disks from Method 1 are incubated for 2 hours at 37° C. and examined under ultraviolet light.

It was found that mycobacteria reacted in the following ways. (*a*) Standard strains of mycobacteria and photochromogenic, non-photochromogenic, and skotochromogenic acid-fast bacilli (45 strains in all) picked up the auramine stains very easily and did not decolorize rapidly in the presence of alkali, giving a bright yellow colour both on the disks and on the solid medium. Fluorescence with Method 3 was either green or yellow-orange against a negative lavender-hued background. These findings agreed with the standard neutral red test except for 3 strains of skotochromogens which differed in the flood and fluorescence tests and one further skotochromogen which differed in the fluorescence test only. (*b*) Non-acid-fast organisms examined, including *Monilia* and fungi, gave a negative result by all three methods of testing. (*c*) A group of miscellaneous acid-fast organisms which were negative by the neutral red test were also negative to auramine, while one saprophyte was positive to both neutral red and auramine. (*d*) A series of 43 strains of tubercle bacilli isolated clinically gave a positive result by all 3 auramine methods. (*e*) Lastly, several positive cultures undetected on routine microscopical examination were revealed by the flood test. The cellular constituent responsible for the reaction is thought to be mycolic acid. *John M. Talbot*

Pharmacology and Therapeutics

581. **Interactions between Pharmacodynamic and Placebo Effects in Drug Evaluations in Man**
W. MODELL and M. GARRETT. *Nature* [*Nature (Lond.)*] **185**, 538–539, Feb. 20, 1960. 7 refs.

To assess the differential effects of pharmacodynamic and placebo action of drug administration a double-blind trial was carried out on 12 male medical students at Cornell University Medical College, New York. The response to sedatives of high-amplitude finger tremor induced by competitive mental work was studied and the trial was conducted with 100-mg. and 50-mg. doses of pentobarbitone, dummy capsules, and with no medication at all. Administration of both the active drug (100 mg.) and the placebo was associated with an increase in the rate of tremor, but the increase was significantly less with the active drug than with placebo; 50 mg. of pentobarbitone produced an effect not significantly different from that of the placebo. When no medication was given the increase in the rate of tremor was again significantly less than with the placebo.

The authors conclude that knowledge of participation in the investigation inevitably led to an increase in the rate of tremor but, although 100 mg. of pentobarbitone increased the rate compared with the period without medication, the results were significantly better than with the placebo capsules. The study indicates the difficulty of assessment of the absolute effects of drug action in view of the difficulty of obtaining a base-line, particularly if placebo effects and drug effects are in the same direction, as the latter may then either supplement the former or merely accompany them. However, if the nature, direction, and magnitude of the placebo effects can be discovered, the base-line can be established and accurate measurement of drug effect can be made. For this purpose the authors suggest the inclusion of a period of no medication in addition to the usual identical placebo in the classic double-blind trial.

Gerald Sandler

582. **Proteolytic Enzymes: a Therapeutic Evaluation.** [Review Article]
S. SHERRY and A. P. FLETCHER. *Clinical Pharmacology and Therapeutics* [*Clin. Pharmacol. Ther.*] **1**, 202–226, March–April, 1960. Bibliography.

583. **Speed of Action of Aspirin, Soluble Aspirin, and Buffered Aspirin**
P. SLEIGHT. *Lancet* [*Lancet*] **1**, 305–307, Feb. 6, 1960. 1 fig., 12 refs.

In an investigation carried out at St. George's Hospital, London, 6 normal volunteers were given 10-grain (0·65-g.) doses of aspirin in each of four forms—aspirin, *B.P.*, calcium aspirin, and two buffered preparations ("bufferin" and "paynocil")—a double-blind technique being used and the drugs being given in predetermined random order. Each dose was given mixed in 6 oz. (170 ml.) of water 2 hours after a normal breakfast. The serum salicylate level was determined on samples of blood removed at intervals up to 30 minutes after ingestion. The mean levels attained in the serum 30 minutes after the administration of bufferin, calcium aspirin, and paynocil were similar, ranging from 4·6 to 5·4 mg. sodium salicylate per 100 ml., whereas it was only 3·3 mg. per 100 ml. for aspirin, *B.P.* Calcium aspirin was therefore as effective in producing a high blood level rapidly as the 2 buffered preparations, and all 3 were superior to plain aspirin. It is suggested that this is attributable to diminished gastric irritation and consequent speedier gastric emptying. *Anne Tothill*

584. **The Mode of Action of Acetylsalicylic Acid (Aspirin) in Man.** (Zur Kenntnis der Wirkung der Acetylsalicylsäure (Aspirin) beim Menschen)
I. ABELIN and W. BERLI. *Schweizerische medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **90**, 87–91, Jan. 23, 1960. 1 fig., 30 refs.

In this communication from the Institute of Medical Chemistry, University of Berne, the authors discuss the observed fact that the administration of 1 to 1·5 g. of acetylsalicylic acid (aspirin) in man produces a marked increase in the urinary excretion of the hormonal catechol amines adrenaline and noradrenaline and of their precursors, such as hydroxytyramine (dopamine). The total amount of catechol excreted in the urine is also significantly increased. The maximum increase usually occurs some 2 to 3 hours after taking the aspirin, the amount excreted then gradually returning to normal.

The authors suggest that the increased blood levels of adrenaline and noradrenaline stimulates the anterior lobe of the hypophysis in its secretion of the adrenal cortical hormone ACTH (corticotrophin), this in turn causing secretion by the adrenal glands of therapeutically valuable steroids, the suggested chain of reaction being: acetylsalicylic acid→adrenaline–noradrenaline→ACTH →cortisone. *L. A. Elson*

585. **Studies of the Mechanism of Action of Chlorothiazide in Cardiac and Renal Diseases. I. Acute Effects on Renal and Systemic Hemodynamics and Metabolism**
A. P. CROSLEY JR., R. C. CULLEN, D. WHITE, J. F. FREEMAN, C. A. CASTILLO, and G. G. ROWE. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **55**, 182–190, Feb., 1960. 18 refs.

In this study of the acute effects of the oral diuretic chlorothiazide on renal and systemic haemodynamics and on metabolism in man, carried out at the University of Wisconsin Medical School, Madison, the glomerular filtration rate, effective renal plasma flow, and blood flow in 14 patients with cardiac or renal disease, or both, were measured for three 15-minute periods before and

for four 15-minute periods after the intravenous injection of 0·7 to 5·0 mg. of chlorothiazide per kg. body weight. The urinary flow, urinary *p*H, and urine and plasma osmolarities and electrolyte concentrations were also determined.

It was found that the glomerular filtration rate and renal blood flow decreased significantly, and that the decreases were coincident with, and probably secondary to, a decline in cardiac output. The fall in cardiac output was associated with a decrease in central venous pressure, which was compatible with a decline in venous return and/or venous pooling. The relationship of these results to those observed clinically after long-term administration of chlorothiazide is discussed.

J. E. Page

586. **Studies of the Mechanism of Action of Chlorothiazide in Cardiac and Renal Diseases. II. Acute Effects on Electrolyte and Acid–Base Metabolism**
A. P. Crosley Jr., R. C. Cullen, D. White, J. F. Freeman, C. W. Crumpton, C. A. Castillo, and G. G. Rowe. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **55**, 191–198, Feb., 1960. 11 refs.

The reaction mechanism responsible for the significant rise in the *p*H and excretion rate of urine after the acute intravenous administration of chlorothiazide has been further investigated, the patients and experimental procedures being the same as those described in the authors' previous paper [see Abstract 585].

From the detailed results of this study, which are tabulated, the authors conclude that chlorothiazide by its action on the proximal tubule produces an increased excretion of sodium and chloride, and by its inhibition of carbonic anhydrase in the distal tubule an enhanced loss of potassium and " buffer base ", as defined by Barker and Elkinton (*Amer. J. Med.*, 1958, **25**, 1). It is suggested that the rise in *p*H of arterial blood, which occurs despite the urinary changes, is related to a transfer of buffer base from the intracellular to the extracellular fluid phase in exchange for hydrogen ions.

J. E. Page

587. **Plasma Pempidine Concentrations in Hypertensives**
C. T. Dollery, D. Emslie-Smith, and D. F. Muggleton. *British Medical Journal* [*Brit. med. J.*] **1**, 521–523, Feb. 20, 1960. 4 figs., 3 refs.

Using an eosin fluorescence technique the authors estimated the plasma concentration of pempidine in 10 hypertensive patients at intervals after administration of varying doses in the fasting state. After a single dose by mouth the plasma concentration of the drug increased rapidly, reaching a maximum in 2 hours, and fell to very low levels within 6 hours. There was a good correlation between the plasma concentration of pempidine and blood pressure. In patients receiving maintenance therapy the plasma level fell more slowly, and correlation between this and the amount of pempidine administered was not as striking as that after a single dose.

The data from the maintenance-dose studies were used to construct standard curves from which the plasma concentration of pempidine could be predicted from the size and the time of administration of the last dose. It was found that in 24 out of 32 patients who were receiving pempidine therapy as a routine the plasma concentration of the drug was within ±50% of the predicted value. Of the 3 patients in whom the plasma pempidine level exceeded that expected by more than 50%, 2 had impaired renal function.

H. F. Reichenfeld

588. **The Influence of Morphine and Pethidine in Combination with Levallorphan on Biliary Duct Pressure after Cholecystectomy**
K. Kjellgren. *British Journal of Anaesthesia* [*Brit. J. Anaesth.*] **32**, 2–6, Jan., 1960. 4 figs., 7 refs.

An investigation was performed on 30 patients undergoing cholecystectomy at the Central Hospital, Gelfe, Sweden, in which, at the end of the operation, a cannula was inserted into the common bile duct or through a choledochotomy and the biliary pressure measured manometrically to an accuracy of 0·5 cm. of water. Only resting pressures were registered, and readings were taken 3 to 5 days after operation.

On successive days 20 patients received 10 mg. of morphine alone and then 10 mg. of morphine together with 0·5 to 2·0 mg. of levallorphan; the remaining 10 patients were given 100 mg. of pethidine, first alone and then with 1·25 mg. of levallorphan. The pressure in the common bile duct was measured at intervals up to 90 minutes after the injection of the drug or drugs.

The author records both the individual and the mean results graphically and demonstrates that the rise in pressure in the biliary ducts induced by morphine or pethidine is significantly decreased by the addition of levallorphan. A further study on patients with cholelithiasis showed an increased frequency of satisfactory cholangiograms after the addition of levallorphan to pethidine compared with the usual premedication with morphine and hyoscine.

Michael Kerr

589. **The Mechanism of Action of Rubefacients**
G. P. Fulton, E. M. Farber, and A. P. Moreci. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **33**, 317–325, Dec., 1959. 6 figs., 17 refs.

The effects of rubefacients on the semi-transparent cheek pouch of the Syrian hamster were assessed directly at Stanford University School of Medicine, San Francisco, by micromanipulatory methods, transillumination, and motion-picture recording with 16-mm. colour film. Dial with urethane provided anaesthesia, while the materials tested included esters of nicotinic acid (ethyl, methyl, n-hexyl, and tetrahydrofurfuryl) in concentrations of 0·1 to 100% in mammalian Ringer's solution, essential oils (mustard, wintergreen, clove, capsicum, turpentine, and camphor), and histamine. Occasionally vasoconstrictive agents—adrenaline, noradrenaline, electric current, or cold Ringer's solution—were used beforehand to induce a standard vessel size if the arterioles were found to be in maximum dilatation.

With all groups of materials a maximal and comparable degree of vasodilatation was achieved regardless of concentration, suggesting an all-or-none response. There

was simultaneous vasodilatation beyond the site of contact of the stimulant, indicating that the vasodilatation produced by rubefacients is mediated by a conducting mechanism with nerve-like properties acting upon smooth muscle units to give the all-or-nothing response. The only differences noted between the various agents were in latent period and duration of response. In a few cases an unexplainted vasoconstriction was obtained with the agents used. The participating vessels included the arterioles, the precapillary sphincters, and the large venules, all of which contain smooth muscle. Capillaries participated only by passive dilatation due to increased blood flow. Local anaesthesia was found to abolish the effects noted above. In 100% concentration all the materials tried produced the classic signs of inflammation. The authors feel that the results suggest that rubefacients act through local perivascular transmission of the vasodilator impulse. *Allene Scott*

590. **"Nesacaine" (2-Chloroprocaine): Its Relative Nontoxicity as Demonstrated by *in vivo* Studies**
F. P. Ansbro, A. E. Blundell, B. Bodell, and J. W. Pillion. *Anesthesia and Analgesia; Current Researches* [*Anesth. Analg. curr. Res.*] **39**, 7–12, Jan.–Feb., 1960. 5 figs., 14 refs.

The *in vivo* and laboratory effect of hydrolysis of chemical compounds with ester and amide linkages was employed in clinical research to determine the least toxic chemical combination available for safe regional anesthesia. "Nesacaine", an ester of 2-chloro-4-aminobenzoic acid and diethylaminoethanol (a 2-carbon aminoalcohol), proved by statistical analysis to be our best agent. Another ester of *para*-aminobenzoic acid, procaine, (also a 2-carbon aminoalcohol), and an ester of benzoic acid, hexylcaine (a 3-carbon aminoalcohol), were more toxic. A drug with an amide linkage (lidocaine [lignocaine]) was the most toxic of the compounds studied *in vivo*.—[Authors' summary.]

591. **The Uptake of Thiopental by Body Tissues and Its Relation to the Duration of Narcosis**
H. L. Price, P. J. Kovnat, J. N. Safer, E. H. Conner, and M. L. Price. *Clinical Pharmacology and Therapeutics* [*Clin. Pharmacol. Ther.*] **1**, 16–22, Jan.–Feb., 1960. 3 figs., 10 refs.

In an investigation reported from the Hospital of the University of Pennsylvania, Philadelphia, the distribution of thiopentone in the tissues after its intravenous injection was studied in 8 patients undergoing operations. The concentration of the drug was measured in samples of brachial arterial blood and of fat excised from the subcutaneous tissue or omentum obtained before and at various intervals after the injection of 150 to 300 mg. of thiopentone. Samples of the rectus muscle were also obtained in 2 cases. Six other patients were studied preoperatively, being anaesthetized with small doses of thiopentone (50 to 100 mg. repeated once or twice) while needles were inserted into the carotid artery and the jugular bulb under local anaesthesia. Blood samples were then taken from these simultaneously at varying intervals after a further injection of 150 to 300 mg. of thiopentone. In some cases the cerebral blood flow was estimated by the nitrous oxide method.

It was shown that although the brain took up thiopentone very rapidly, its content reaching a peak of 10% of the dose in less than one minute after the end of the injection, only half of the peak content remained 5 minutes later and in 20 minutes only one-tenth remained. Fat concentrated thiopentone to a very small extent during this period and was considered not to be responsible for depleting the brain. But the equilibration of thiopentone between the blood and the lean tissues was found to occur rapidly enough to account for its rapid removal from the brain. The distribution of thiopentone between the various areas of the body was predicted mathematically from the rate of perfusion per unit mass and the concentration ratio between tissue and blood of thiopentone in these areas at equilibrium. There was a high order of agreement between these results and the experimental findings.

The ultra-short action of thiopentone has hitherto been thought to be due to its concentration in the body fat. It would now appear that fat plays a smaller role than was supposed and that the rate of recovery from thiopentone anaesthesia depends to a greater extent than has been recognized on the mass of the body and the rate at which its tissues are perfused. *M. Woods*

592. **Drugs Which Stimulate Affective Behaviour. I. Action of Lysergic Acid Diethylamide (LSD-25) against Thiopentone Anaesthesia in Dogs**
A. B. Dobkin and J. H. Harland. *Anaesthesia* [*Anaesthesia*] **15**, 48–54, Jan., 1960. 1 fig., 13 refs.

The analeptic effect of lysergic acid diethylamide (LSD-25) on dogs anaesthetized with thiopentone was studied at the University of Saskatchewan College of Medicine and the University Hospital, Saskatoon. A sleep dose of thiopentone was given to 6 dogs, which were then intubated and thereafter ventilated with oxygen by a positive–negative pressure respirator set at 30 to 35 cycles per minute and 3 to 4 litres minute volume. Electrocardiograms, electroencephalograms, pneumotachygrams, and arterial blood pressure were recorded continuously throughout each experiment. After control recordings had been obtained an estimated lethal dose of thiopentone (75 to 125 mg. per kg. body weight) was given rapidly by intravenous injection. When cardiovascular depression became evident 50 to 100 μg. of LSD-25 per kg. body weight was injected. Only one of the dogs died; in the remainder a period of 80 to 170 minutes elapsed before respiration and blood pressure gradually began to return.

To a further 10 animals 25 mg. of thiopentone per kg. body weight was given at 4-weekly intervals, and on each occasion alternate groups of 5 dogs were given 25 μg. of LSD-25 per kg. one minute after the thiopentone. After the injections the dogs were allowed to recover undisturbed. The apnoea which followed the administration of thiopentone was not always immediately reversed by LSD-25 and there was no significant improvement in recovery time with LSD-25.

Mark Swerdlow

Chemotherapy

593. **The Clinical Use of an Epoxide Alkylating Agent, Epoxypropidine, in Neoplastic Disease**
D. G. MILLER, H. D. DIAMOND, and L. F. CRAVER. *Clinical Pharmacology and Therapeutics* [*Clin. Pharmacol. Ther.*] **1**, 31–38, Jan.–Feb., 1960. 3 figs., 6 refs.

A study was made at the Memorial Center for Cancer and Allied Diseases, New York, of the use of epoxypropidine (1:1′-bis-(2:3-epoxypropyl)-4:4′-dipiperidyl) as a cytotoxic agent in the treatment of 30 patients suffering from various types of inoperable malignant disease (Hodgkin's disease, lymphosarcoma, reticulum cell sarcoma, mycosis fungoides, chronic myeloid leukaemia, and carcinomatosis). The compound was dissolved in normal saline in a concentration of 10 mg. per ml. and injected into the tubing of a fast-running intravenous infusion of 5% glucose in distilled water. A dose of 5 mg. per kg. body weight was observed to induce leucopenia and thrombocytopenia of the degree and duration usually seen with 0·4 mg. of nitrogen mustard per kg. Where marrow function was diminished for any reason smaller doses (2 to 3 mg. per kg.) were used. A dose sufficient to cause a fall in the leucocyte count to less than 4,000 per c.mm. was considered to be adequate and was given to 21 patients. A positive result was recorded when a measurable area of disease decreased by one-third or more provided that no other area of disease was increasing at this time. The effect was also assessed by means of the temperature response, radiography, and haematological and biochemical studies when appropriate. The response of the disease was correlated with the response of the patient by an estimation of his " performance status " according to the method of Karnofsky and Burchenal (*Clinical Evaluation and Chemotherapeutic Agents in Cancer*, New York, 1949).

In 7 out of 9 cases of Hodgkin's disease symptoms diminished and the performance status improved. Various responses were observed, but there was no significant effect on pleural effusion in 2 cases or on skin infiltration in a third. The duration of improvement varied from 1 to 5 months; 2 cases are reported in detail in which the patients are still slowly improving. Four patients with lymphosarcoma received 5 courses of epoxypropidine; of these, 3 showed subjective and one clinical improvement. The case histories are presented in detail; 2 of the patients died from other causes, one had signs of recurrence after 14 weeks of improvement, and one was still improving after 10 weeks of therapy. Short-term improvement occurred in the 3 patients suffering from reticulum cell sarcoma who were treated with epoxypropidine. No amelioration of symptoms occurred in one case of mycosis fungoides, one of chronic myelogenous leukaemia, or 3 of disseminated carcinoma from primary disease of the lung, ovary, and breast respectively.

Epoxypropidine thus produces some improvement in neoplastic disease of the reticulo-endothelial system, but it apparently has no specific effect on the more commonly encountered disease of carcinomatosis. The authors found no evident therapeutic advantage over epoxypropylpiperazine or nitrogen mustard. *Anne Tothill*

594. **Antipenicillinase Serum: Use in Treatment of Resistant Staphylococcal Infections in Laboratory Animals**
W. E. WICK, D. H. HOLMES, and W. S. BONIECE. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **10**, 71–77, Feb., 1960. 24 refs.

It is now generally accepted that the resistance of staphylococci and other pathogens to penicillin is due to the production of penicillinase by the organisms. It has been shown that when an antiserum which can neutralize penicillinase is given to animals it enables treatment with penicillin, which would otherwise fail, to become effective. Similarly, it is possible to produce an active immunity by inoculation with penicillinase. These techniques have not yet been attempted in man.

In the present paper the authors describe some of their experiments in the production of penicillinase immunity carried out at the Lilly Research Laboratories, Indianopolis. Rabbits were immunized with penicillinase obtained from *Bacillus cereus* and also from a resistant strain of *Staphylococcus aureus*. The titres obtained with the latter were significantly higher than with the former, suggesting an immunological difference between the types of penicillinase produced by the two organisms. In further experiments groups of mice were given antipenicillinase serum 2 hours before intravenous infection with staphylococci, control groups being given normal serum. Some of the test groups were given penicillin before infection and others the antibiotic at various times after infection, the effect of such therapy being measured by counting the staphylococcal population in homogenized kidney tissue on the 2nd, 3rd, and 4th days after infection. The results showed that the antiserum was beneficial in preventing staphylococcal infection if the antibody and penicillin were present before or very shortly after infection. However, if the first dose of penicillin was not given until 5 hours after infection the antiserum had no beneficial effect.

Finally an experiment was performed on rabbits to compare the effects of active and passive immunity, the survival time of the animals being taken as a measure of the effectiveness of the methods. Rabbits immunized either actively or passively survived longer than those treated with penicillin alone, but the results were not conclusive as some of the animals treated with antiserum died, while one rabbit which received penicillin only recovered. It is thought that more consistent results might be obtained if the infecting dose of staphylococci was adjusted more accurately to the weight of the animal and if a purified antiserum was used.

R. F. Jennison

Infectious Diseases

595. **Dog-bites and Local Infection with *Pasteurella septica***
M. L. H. Lee and A. J. Buhr. *British Medical Journal* [*Brit. med. J.*] **1**, 169–171, Jan. 16, 1960. 9 refs.

The incidence and therapeutic management of infected dog-bites were studied at the Radcliffe Infirmary Oxford. Bacteriological investigation of the wound in 69 patients who had been bitten by a dog revealed frank infection in 20, which included 14 of the 30 wounds in the series which had been sutured. *Pasteurella septica* was cultured from 12 of the 69 wounds and 10 of these showed frank infection, thus accounting for 50% of all the infected wounds. Prophylactic penicillin appeared to be successful, because an infected bite developed in only one out of 9 patients given the antibiotic. In view of this and of the fact that infected bites require prolonged treatment and leave unsightly scars the authors suggest that prophylactic penicillin should be given in all cases of severe dog-bite. *Winston Turner*

596. **Experience with Amphotericin in the Therapy of Histoplasmosis**
J. L. Yates, M. N. Atay, H. V. Langeluttig, C. A. Brasher, and M. L. Furcolow. *Diseases of the Chest* [*Dis. Chest*] **37**, 144–156, Feb., 1960. 2 figs., 15 refs.

Amphotericin B, an antibiotic produced by a strain of *Streptomyces* originally isolated from a soil sample in South America, has negligible antibacterial action but is a potent broad-spectrum antifungal agent and seems to be the most valuable drug now available for the treatment of deep mycoses. Unfortunately it frequently produces toxic effects and hypersensitivity states similar to those caused by other antibiotics; also it is effective only when given intravenously and for periods of at least 8 to 16 weeks. In this paper the results obtained with the antibiotic in the treatment of pulmonary histoplasmosis are reported from the Missouri State Sanatorium at which, lying as it does on the edge of a highly endemic area, a considerable experience of this condition has been built up. The average daily dosage was 0·75 mg. per kg. body weight in 5% glucose solution.

Of the 29 patients treated (27 men and 2 women, all of the white race and of an average age of 53 years), 27 had active pulmonary histoplasmosis with cavitation, while in the remaining 2 the disease was widely disseminated. Culture of the sputum was positive for histoplasmosis in 27 cases; tuberculosis was ruled out by negative gastric cultures and negative tuberculin tests. The results of treatment were generally favourable, with striking improvement in the general condition (initially particularly poor in 10 cases), a marked decrease in the amount of sputum, conversion of positive sputum to negative, and reduction in the titre of the complement-fixation test. Radiological changes, however, were less impressive, although considerable clearing of the lungs was seen in the one acute benign case and both disseminated cases. Side-effects were noted in most patients, but discontinuance of the drug was necessary in only 3; toxic effects consisted in pyrexia, skin rashes, phlebitis around the site of the intravenous injection without, however, development of thrombosis, and a considerable rise in the blood urea nitrogen level in 3 cases. Many of the side-effects were controlled by the addition of hydrocortisone to each intravenous infusion, and the addition of 25 mg. of heparin appeared to prevent venous thrombosis. The duration of treatment ranged from 6 to 22 weeks. During the period of follow-up, which extended to 24 months in some cases, several relapses occurred and second or even third courses of treatment have been necessary. Evidence of development of fungal resistance to amphotericin B and nystatin was observed and is to be the subject of a further study. *A. J. Karlish*

597. **Viremia in Infection Due to ECHO Virus Type 9**
I. Yoshioka and D. M. Horstman. *New England Journal of Medicine* [*New Engl. J. Med.*] **262**, 224–228, Feb. 4, 1960. 3 figs., 14 refs.

Viraemia during the course of infections due to ECHO viruses has been reported in a few cases only. In this paper from Yale University School of Medicine, New Haven, Connecticut, the authors describe the occurrence of viraemia in children suffering from infection due to ECHO virus Type 9. The infection occurred in June, 1958, among children living in one of the cottages of an institution for the retarded. Of the 57 inmates, aged 6 to 12 years, 4 developed aseptic meningitis and 42 had fever and malaise; 11 were asymptomatic. From 18 of the children blood samples which had already been taken for other, unrelated, serological studies were examined. ECHO virus Type 9 was isolated from blood specimens from 2 children who remained afebrile, 7 out of 15 who developed symptoms up to 5 days later, and one child in whom fever and signs of central nervous system involvement developed 3 and 5 days later respectively. Convalescent sera taken a month later showed a 4-fold rise in neutralizing antibody titre.

ECHO virus Type 9 was isolated from various other specimens collected from 29 children during the epidemic, as follows: 27 out of 29 stool specimens, 7 out of 8 throat swabs, and one out of 3 specimens of cerebrospinal fluid from cases of meningitis. Neutralizing antibody titres of 1:50 to 1:1,250 or greater were found in 54 of 55 samples of serum taken one month later. Of 15 children re-tested 3 months after the outbreak, 10 showed no change in antibody titre, 3 an increase in titre, and 2 a decrease. The complement-fixing antibody response showed a similar general pattern.

A strain of ECHO virus Type 9 isolated in 1957 was fed to 2 chimpanzees. Viraemia was detected from the 4th up to the 8th day in one animal, which developed fever, and on the 2nd day only in the other animal, which remained well. The virus was recovered from throat

swabs from both chimpanzees up to the 17th day and from the stools during the first 3 days only. There was a significant rise in neutralizing antibody titre in both animals.

The findings indicate that viraemia probably occurs commonly in infections due to ECHO virus Type 9 and precedes clinical disease. The authors discuss the pattern of infection due to ECHO Type 9 and poliomyelitis viruses and the pathogenesis of disease with these two enteric agents. *Joyce Wright*

BACTERIAL DISEASES

598. **Bacteraemia in Human Brucellosis**
W. GANADO and W. BANNISTER. *British Medical Journal* [*Brit. med. J.*] **1**, 601–603, Feb. 27, 1960. 10 refs.

The incidence of bacteriaemia in brucellosis was studied in 93 cases of the disease admitted to St. Luke's Hospital, Malta. *Brucella melitensis* was cultured from the blood in 74 cases by Castaneda's method, in which tryptose broth and agar were used. Samples of blood and of marrow (from the sternum) from 35 cases were also cultured. Both blood and marrow were positive for *Br. melitensis* in 16 cases and both were negative in 5. In 7 cases marrow culture only was positive; in the remaining 7 blood only was positive. Thus in some cases the results of marrow culture may assist in establishing the diagnosis.

In a further study of the connexion between pyrexia and bacteriaemia it was found that *Br. melitensis* may be present in the blood stream even when the patient is apyrexial. It is therefore suggested that pyrexia is due not so much to pyrogen from the organisms themselves as to substances having this type of action coming from the cells of the host. *R. Hare*

599. **Total Paralysis Regime in Severe Tetanus**
S. M. A. ALHADY, D. P. BOWLER, H. A. REID, and L. T. SCOTT. *British Medical Journal* [*Brit. med. J.*] **1**, 540–545, Feb. 20, 1960. 4 figs., 10 refs.

The results obtained with the total paralysis regimen (T.P.R.) in the treatment of severe tetanus are described in this paper from the General Hospital, Penang, Malaya. All the patients, 6 children (over 2 years of age) and 4 adults, had had one or more tetanic spasms severe enough to stop respiration. The usual prognostic indices of severity—short incubation period and brief duration of onset—were found to be unreliable in this series, since in 4 of the patients the incubation period was 7 days or more and in all except 3 the period of onset was 24 hours or longer.

The T.P.R. included preliminary administration of atropine, thiopentone, and suxamethonium intravenously, oral intubation, tracheostomy followed by the passage of a "polythene" stomach tube, intermittent positive-pressure respiration, and curarization; D-tubocurarine was given intravenously at first and then intramuscularly, together with hyaluronidase, in a dosage of 4 to 30 mg. every 1 to 2 hours day and night for 2 to 12 days.

Only 2 of the patients (aged 11 and 14 years respectively) survived; in a further case the T.P.R. was probably stopped prematurely, the patient dying from a lung infection 10 days later. Since hypotension was present in all the fatal cases together with electrocardiographic signs of myocardial insufficiency it was considered that central myocardial failure was the principal cause of death. This view was supported by the systolic blood pressure response to digoxin but not to noradrenaline in one case and the histological evidence of toxic myocarditis (similar to that in diphtheria) in another in which death occurred after T.P.R. for 3 days and hypotension for 2. It is concluded that direct toxic myocardial damage may cause death in certain very severe cases of tetanus, no matter how successful are the measures for preventing tetanic spasms and maintaining respiration. [This is an excellent report.]
H. Stanley Banks

600. **Effects of Diphtheria Toxin on Acetylcholine Synthesis**
S. C. AGARWAL. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **79**, 313–318, 1960. 7 refs.

Since the author has shown experimentally that diphtheria toxin does not block the transmission of impulses at the neuro-muscular junction in the rat phrenic-nerve–diaphragm preparation or appear to interfere with cholinesterase production it was thought that its paralytic effect might instead be due to its inhibition of the synthesis of acetylcholine. In experiments carried out at the Wright–Fleming Institute of Microbiology, St. Mary's Hospital, London, in an attempt to confirm this, slices of rat brain were incubated in eserinized glucose–phosphate saline, with and without varying amounts of the purified protein fraction of diphtheria toxin, the amount of bound and free acetylcholine produced being estimated by its effect on eserinized frog muscle or chemically by its interaction with hydroxylamine.

The addition of 500 guinea-pig MLD of the toxin to the reaction mixture was found to reduce the total amount of acetylcholine synthesized in 3 hours by 40 to 80%. With smaller doses (10 to 100 MLD) of toxin the amount of the free form of acetylcholine was still reduced, but the total yield less so. From experiments with ether, which sets bound acetylcholine free, it was found that the toxin did not interfere with the actual liberation of acetylcholine. Again, as the yield of acetylcholine was not diminished by adding toxin to a choline acetylating system, it seems that the toxin does not inhibit the synthetic mechanism directly, that is, by inhibiting the acetylation of co-enzyme A. The author therefore concludes that the toxin must reduce the synthesis of acetylcholine in the nerve cells by interfering with the production of some essential substrate, such as choline or acetate. *Janice Taverne*

601. **Bacterial Infections of Animals Transmissible to Man.** [Review Article]
L. W. MACPHERSON. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **239**, 347–362, March, 1960. Bibliography.

Tuberculosis

602. **The Tuberculin Test and the Diagnosis of Clinical Tuberculosis**
W. W. JOHNSTON, H. A. SALTZMAN, J. H. BUFKIN, and D. T. SMITH. *American Review of Respiratory Diseases* [*Amer. Rev. resp. Dis.*] **81**, 189–195, Feb., 1960. 21 refs.

Investigation of patients with bacteriologically proved tuberculous infection using various strengths of purified protein derivative (P.P.D.), tuberculin, and old tuberculin (O.T.) have shown that a high proportion failed to react to intermediate strength P.P.D. (5 T.U.) or to O.T. 1 in 100. The authors report that at the Veterans Administration Hospital, Durham, N. Carolina, 4 (4·9%) of 81 patients reacted to second strength P.P.D. only and one patient (1·2%) failed to react at all, while the proportion of patients failing to react to 1 in 1,000 O.T. was as high as 34% at the neighbouring Duke Hospital and 15 of 94 patients (16%) failed to react at all to 1 in 100 O.T.

The subsequent administration of increasing doses of P.P.D. to healthy medical students confirmed that a reaction due to chemical irritation occurred only with very high strengths of P.P.D. (0·5 mg.), which was marked at 6 hours, maximum at 24 hours, and had practically disappeared by 48 hours. Patients infected with atypical acid-fast bacilli may have induration of 10 mm. or more in diameter with 5 T.U. of P.P.D. (0·0001 mg.), but generally react only with second strength (0·005 mg.) P.P.D. Healthy subjects reacting only to second strength are more resistant to the development of clinical infection than any other group. *John M. Talbot*

603. **Intermediate-strength Purified Protein Derivative: Its Diagnostic Significance in Active Tuberculosis**
S. KATZ, R. C. DUVALL, T. J. RYAN, T. F. O'CONNOR, R. J. MARILLY, and R. B. PERRY. *American Review of Respiratory Diseases* [*Amer. Rev. resp. Dis.*] **81**, 196–199, Feb., 1960. 1 fig., 8 refs.

When 416 patients with proven tuberculosis were examined at either the District of Columbia General Hospital, Washington, D.C., or the Baltimore Veterans Administration Hospital with intermediate strength P.P.D. (0·0001 mg. or 5 T.U.) it was found that a positive reaction was given by 386 (92·8%) of them at the first injection. A positive reaction was defined as an area of induration of at least 5 mm. in diameter at the site of injection within 48 to 72 hours. When the 30 patients initially showing a negative result were retested with the same dose 23 of them now gave a positive reaction. Closer study of the remaining 7 patients showed that in 6 of them there was an obvious cause for anergy, such as very advanced disease or the administration of steroids. In the 7th patient no obvious cause for the negative finding could be established. Excluding these exceptional cases, the authors conclude that the skin test with an intermediate dose of P.P.D. gives an accurate result in 99·76% of cases, provided it is repeated in initially negative cases and causes of technical error or misreading are excluded. *John M. Talbot*

604. **Treatment of Pulmonary Tuberculosis with Large Doses of Isoniazid.** (Traitement de la tuberculose pulmonaire. Les doses " fortes " d'isoniazide)
É. BERNARD, A. P. JARNIOU, L. ISRAEL, M. ENJALBERT, and C. FABRE. *Presse médicale* [*Presse méd.*] **68**, 209–211, Feb. 6, 1960. 35 refs.

In a joint study carried out at the Hôpital Laennec and the Hôpital Percy, Paris, 114 patients with pulmonary tuberculosis were treated with isoniazid in a high dosage of 15 mg. per kg. body weight daily, 90 similar patients who received the customary dosage of 5 mg. per kg. daily serving as a control group; allocation of the patients to one or other group was by chance. In addition both groups received 15 g. of PAS intravenously daily, and patients in the high-dosage group were also given pyridoxine, 200 mg. intramuscularly thrice weekly.

After 3 months' treatment there was significant radiological improvement in 50·8% of the high-dosage group compared with 38·8% of the normal-dosage group. In the former group this improvement was more obvious in the patients with extensive or cavitating disease than in those with less extensive, nodular, or infiltrating lesions. In this group also the sputum became negative for tubercle bacilli more quickly and more frequently than in the low-dosage group. In only one patient receiving the higher dosage had treatment to be discontinued because of mental excitement, and this was reversible. The authors consider that neuropsychical accidents during isoniazid therapy are more frequent in subjects with a previous history of neurosis, to whom, they suggest, pyridoxine should therefore be given prophylactically as a routine. *I. Ansell*

605. **Prolonged Drug Treatment for Pulmonary Tuberculosis**
J. BATTEN, M. TURNER-WARWICK, C. HOYLE, and H. NICHOLSON. *Lancet* [*Lancet*] **1**, 409–412, Feb. 20, 1960.

There are two outstanding problems in the treatment of pulmonary tuberculosis—namely, how long should each case be treated with antituberculous drugs and how effective is this in preventing future relapse. The authors make some attempts to solve these by assessing the progress of 193 patients who, before June, 1955, had received chemotherapy for at least 9 months; 80 had had chemotherapy for more than 18 months. Of the 193 patients, 134 had been followed up for more than 3 years.

Sputum conversion occurred in almost every case, although in some it was delayed for several months. Of 60 patients with cavities who were treated by drugs alone, the cavities closed in less than 6 months in 30. In a further 19 cavities closed after persisting for 6 months

to 3 years. It is pointed out that persistent cavitation with a positive sputum still carries a very poor prognosis, Of the 193 patients, 182 survived and 174 are now leading normal lives. However, a relapse occurred in 23, some of whom had had chemotherapy for 18 months. Drug resistance was a negligible factor in the relapse rate. The authors state that the period for which drugs should be given " remains obscure ", but they strongly favour a minimum of 2 years, even in the " mild " case. Inadequate chemotherapy in a new case may predispose to drug resistance. They emphasize that out-patients frequently fail to take the drugs prescribed, generally because of the gastro-intestinal symptoms caused by PAS.

Paul B. Woolley

606. **Pneumonectomy in the Treatment of Pulmonary Tuberculosis: the After History**

C. J. MARTIN and W. T. MILLER. *American Review of Respiratory Diseases* [*Amer. Rev. resp. Dis.*] **81**, 184–188, Feb., 1960. 1 fig., 11 refs.

An account is given of the after history of 204 patients who were subjected to pneumonectomy for the treatment of pulmonary tuberculosis at the Firland Sanatorium, Seattle, during the period January, 1946, to June, 1955. All of them had bilateral disease and in 39% it was at least moderately advanced on the unoperated side. They were divided into three groups as follows: (1) 54 (26%) who had undergone a previous thoracoplasty; (2) 134 (66%) who were treated by concomitant thoracoplasty; and (3) 16 (18%) who did not have thoracoplasty at all.

It was shown that at the first anniversary of the performance of pneumonectomy a patient had a 60% chance of having inactive disease and a 24% chance of having active disease; 11% were dead and the residue lost to follow-up. At the eighth anniversary of the operation 63% were found to have inactive disease, none had active disease, and 21% were dead of their tuberculosis or from causes related to the pneumonectomy. None of the patients treated by pneumonectomy without thoracoplasty had been followed for more than 3 years; but with this reservation the outcome of the pneumonectomy was not influenced by previous or concomitant thoracoplasty. When compared with similar patients treated by sanatorium care only the patients treated by pneumonectomy had a much better prognosis. Comparison of the results in the latter with those in patients treated by thoracoplasty alone showed that at the first anniversary the disease was inactive in more pneumonectomized patients than in thoracoplasty patients—60% as against 49%. On the other hand at the third anniversary a greater number of thoracoplasty patients can be expected to have inactive disease—73% as against 68%—but at the same time a greater proportion of active cases (18%) was found in the thoracoplasty group than in the pneumonectomy group (5%). The number of deaths from tuberculosis at the first anniversary is expected to be higher in pneumonectomy cases (11% as against 4%), but by the eighth anniversary pneumonectomy resulted in only a slighter greater mortality (21% as against 16%). The authors point out that some of the differences are undoubtedly explained by the fact that thoracoplasty was performed for less advanced disease; thus of the thoracoplasty group as a whole, 21% had no disease on the opposite side.

It is interesting to note that the number of patients who were untraced increased at a fixed rate of 3% per year for the first two anniversaries, and then fell to between 1 and 2% for the 3 succeeding years; after the 5th anniversary the attendance was constant.

Kenneth M. A. Perry

607. **The So-called Resensitization by Treatment of Infecting Mycobacterial Populations Which Have Become Resistant to Antibiotics and Chemotherapeutic Agents.** (La cosidetta resensibilizzazione da terapia delle popolazioni micobatteriche infettanti divenute chemioantibiotico-resistenti)

G. DADDI and M. CORDA. *Giornale italiano della tubercolosi* [*G. ital. Tuberc.*] **14**, 3–13, Jan.–Feb., 1960. 12 figs., 11 refs.

The important question of so-called resensitization of resistant tubercle bacilli has been studied at the Tuberculosis Clinic of the University of Milan. The drug sensitivity of these organisms to streptomycin, isoniazid, PAS, cycloserine, pyrazinamide, kanamycin, and ethionamide was tested every 60 to 90 days in respect of 1,177 sputum-positive patients with pulmonary tuberculosis admitted to the clinic during a period of 2 years. The term resensitization is used to mean that organisms which have developed resistance in the course of antibacterial treatment are later found to be again sensitive to the same drug.

The authors point out the various combinations of antituberculous drugs which apparently favour this process of resensitization. Laboratory reports of drug sensitivity did not always coincide with the clinical progress of the patient, and further clinical improvement was in some cases obtained in spite of continuation of treatment with the drugs to which the patient's organisms were reported to be resistant.

[This process of resensitization obviously cannot be very complete as the authors admit in the text that of the 144 resensitized patients who continued treatment, 18% improved, 75% remained stationary, and 7% became worse. Unfortunately the graph purporting to illustrate these figures seems to show just the opposite, namely, that only 7% improved and 18% became worse.]

A. J. Karlish

608. **Tuberculosis of the Mouth and Throat, with Special Reference to the Incidence and Management since the Introduction of Chemotherapy**

R. A. CAWSON. *British Journal of Diseases of the Chest* [*Brit. J. Dis. Chest*] **54**, 40–53, Jan., 1960. 43 refs.

The author of this paper from the Department of Oral Medicine, King's College Hospital Medical School, London, describes 6 new cases of tuberculosis of the mouth and 8 of tonsillar tuberculosis. The features of 5 different types of tuberculosis of the mouth and throat are discussed with reference to 34 cases reported in the literature. The response to chemotherapy is good, but the author emphasizes that several antibiotics must be given and treatment prolonged for at least 18 months.

B. Golberg

Venereal Diseases

609. **Reproducibility of Results Obtained by the *Treponema pallidum* Immobilization Test in South Africa**
V. BOKKENHEUSER and N. J. RICHARDSON. *South African Journal of Medical Sciences* [*S. Afr. J. med. Sci.*] **24**, 109–113, Dec., 1959 [received May, 1960]. 1 fig., 16 refs.

610. **Evaluation of tpcf-50 Test and Other TPCF Tests for Syphilis Diagnosis**
H. N. BOSSAK, W. P. DUNCAN, A. HARRIS, and V. H. FALCONE. *Public Health Reports* [*Publ. Hlth Rep. (Wash.)*] **75**, 130–134, Feb., 1960. 13 refs.

The antigen used in the tests described in this report from the Venereal Disease Research Laboratory, Chamblee, Georgia, was prepared by the method of Portnoy and Magnuson (*J. Immunol.*, 1955, **75**, 348; *Abstr. Wld Med.*, 1956, **19**, 442) from virulent *Treponema pallidum*. Three complement-fixation methods were employed: (1) TPCF I, a fifth-volume Kolmer method using 1½ exact doses of complement; (2) TPCF II, a similar method, but using four 50% haemolytic doses; and (3) tpcf-50, a micro-method using six 50% haemolytic doses. The results were compared with those of the treponemal immobilization (T.P.I.) test carried out on the same specimens of serum.

The first group of sera came from 326 healthy patients who were presumed to be non-syphilitic. Nine sera were reactive to the T.P.I. test, but Methods 1, 2, and 3 gave 44, 70, and 45 reactive results respectively. [Positive and doubtful results are classed together as reactive.] Method 3 alone was used to examine a further 263 sera from the same category of patients; 15 reactive results were obtained, the T.P.I. reaction on these 15 sera being negative in 12 cases, positive in 2, and weakly positive in one.

The second group of 477 sera came from patients with syphilis at various stages, both treated and untreated. In early syphilis the three complement-fixation tests were considerably more sensitive than the T.P.I. test, Method 3 being the most reactive. In contrast, all three tests were found to be less sensitive than the T.P.I. test with sera from patients with treated latent or late syphilis. All four tests gave comparable results with 86 sera from patients with yaws or pinta.

The last group of sera came from 220 patients classed as biological false positive reactors with lipoidal antigen tests. In 111 instances the diagnosis had been reached because the T.P.I. reaction had previously been found negative. On re-testing it was found positive in 5 instances, while Methods 1, 2, and 3 were reactive in 11, 14, and 10 cases respectively. In the remaining 109 patients the diagnosis of a biological false positive reaction had been made on clinical grounds without a preliminary T.P.I. screening. The T.P.I. test was reactive with 38 sera and Methods 1, 2, and 3 with 44, 47, and 34 sera respectively.

[The high incidence of reactivity of the complement-fixation tests in presumed non-syphilitic patients is surprising and may raise doubts as to their specificity.]

A. E. Wilkinson

611. **Fluorescent Antibody Tests for Detection of the Gonococcus in Women**
W. E. DEACON, W. L. PEACOCK JR., E. M. FREEMAN, A. HARRIS, and W. L. BUNCH JR. *Public Health Reports* [*Publ. Hlth Rep. (Wash.)*] **75**, 125–129, Feb., 1960. 2 figs., 6 refs.

The results are reported from the Venereal Disease Research Laboratory, Chamblee, Georgia, of the examination of female contacts of men with gonorrhoea by conventional cultural methods and by the fluorescent antibody technique described by Deacon *et al.* (*Proc. Soc. exp. Biol.*, 1959, **101**, 322; *Abstr. Wld Med.*, 1960, **27**, 17). Specimens were taken from the urethra, cervix, and vagina and plated on " difco " GC medium base with haemoglobin and Supplement B. Two fluorescence techniques were used; in the direct method films of secretion were prepared from the three sites, fixed, and " stained " with anti-gonococcal serum conjugated with fluoresceine *iso*thiocyanate. In the delayed method the secretions were first cultured on slopes of medium for 16 to 20 hours and thick smears of the mixed growth exposed to the fluoresceine-labelled antibody. The recognition of *Neisseria gonorrhoeae* by either fluorescence procedure was considered to afford complete identification.

In the first group of 50 women examined cultures were positive from a total of 67 sites compared with 22 by the direct and 71 by the delayed fluorescence procedure. Surprise is expressed at the high proportion of positive results obtained from vaginal secretions, gonococci having been demonstrated in 24 cases by culture and the delayed method and in 13 by the direct technique. The two fluorescence procedures were also compared in tests on a further 100 female contacts with gonorrhoea. Gonococci were demonstrated in 24 sites in 24 patients by the direct method and in 128 sites in 58 patients when the delayed method was used.

The authors point out that the use of fluorescence techniques for the detection of the gonococcus offers the big advantage of a more speedy diagnosis and economy in materials and labour.

[From the figures provided the direct technique is clearly much inferior to conventional cultures, while the delayed method gave only slightly better results in the small number of patients in whom comparison of the three methods was made. It is not stated whether cross-reactions may be found with the other *Neisseriae* which may sometimes be found in the female genital tract.]

A. E. Wilkinson

Tropical Medicine

612. **Idiopathic Lymphoedema of Ethiopia and Kenya**
L. B. COHEN. *East African Medical Journal* [*E. Afr. med. J.*] **37**, 53–74, Feb. [received April], 1960. 15 figs., 18 refs.

The author describes 32 cases of idiopathic lymphoedema of the legs, of which 19 were seen in Ethiopia in 1952–4 and 13 in Kenya between 1955 and 1958; only 10 of the patients were female. The condition of idiopathic lymphoedema does not extend above the knee and in most cases a characteristic fine papillomatous outgrowth develops around the edges of the foot and on the toes and heels—an appearance which in East Africa has led to it being called " mossy foot ". In nearly all patients barnacle-like warts are to be found on the dorsum of the foot and on the lower part of the leg when the disease is well established. The presence of filariasis was excluded in these patients. Serial injection of dye preoperatively in 3 cases and x-ray lymphangiography in 13 showed there to be either aplasia or hypoplasia of the lymphatic vessels of the diseased legs. This is believed to be the cause of the condition, the underdeveloped lymphatic system being unable to meet the demands of adult life. The disease is not hereditary or contagious. The repeated traumata to which the feet and lower legs of the bare-footed natives are exposed most probably play some part in causation and it is considered that the condition would become rare if all Africans wore boots.

In the early stages the wearing of boots and antibiotic treatment may prevent further progress of the disease. In late cases, in which elephantiasis has developed, operation by excision of all of the thickened skin, subcutaneous tissue, and deep fascia of the foot and leg is recommended. The skin of the flexor, extensor, and peroneal retinaculae is preserved. Two weeks later the bare area is covered by split skin grafts taken from the thigh. The author describes operations of varying degree which were performed on 22 of these patients. The results were considered to be good in 9 cases, to have brought some improvement in a further 9, and to be fair in 4. The relevant literature is briefly reviewed.

R. R. Willcox

613. **Studies on the Epidemiology of Sleeping Sickness in East Africa. II. Sleeping Sickness in Kenya**
K. R. S. MORRIS. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. roy. Soc. trop. Med. Hyg.*] **54**, 71–86, Jan., 1960. 4 figs., 20 refs.

In a previous paper (*Trans. roy. Soc. trop. Med. Hyg.*, 1959, **53**, 384; *Abstr. Wld Med.*, 1960, **27**, 368) the author described an outbreak of sleeping sickness in Uganda. In this further paper he presents a detailed account of the epidemiology of Gambian sleeping sickness in Kenya based on the earlier records and on his study of the situation in recent years. The disease is restricted to the Nyanza Province, where it was first introduced from Uganda in 1902, and then spread along the shores of Lake Victoria to the borders of the then German East Africa (now Tanganyika), decimating the population. Between 1909 and 1912 this epidemic came to an end as the result of the retreat of the people away from the lake shores, thereby breaking contact with the vector (*Glossina palpalis*) and its riparian habitat. However, the disease continued to spread inland in low endemic form, and between 1920 and 1930 outbreaks occurred again, but by this time the epidemic could be checked by chemotherapeutic measures (" Bayer 205 " and trypars-amide). Further epidemics developed in 1943 and 1954, the disease having spread along the river banks. In some areas the outbreaks were successfully controlled by elimination of the vector with dicophane (DDT) and by clearing vegetation along the shores. At present Gambian trypanosomasis is at a low endemic level, though still persisting in riparian foci.

In discussing the epidemiology of sleeping sickness in Kenya in the light of the foregoing data the author concludes that " the present period of very low endemicity offers a unique opportunity for the complete eradication of *T. gambiense* from this part of Kenya ".

C. A. Hoare

614. **The Value of Thiacetazone (TB-1) in Leprosy**
A. M. ALONSO. *International Journal of Leprosy* [*Int. J. Leprosy*] **27**, 321–327, Oct.–Dec., 1959 [received March, 1960]. 8 refs.

From the Institute of Leprology, Rio de Janeiro, the author discusses the treatment of leprosy with TB–1 (thiacetazone), a thiosemicarbazone originally introduced by Domagk for the treatment of tuberculosis. Although a number of favourable reports of its action in leprosy appeared between 1949 and 1952, the drug was never widely used and was gradually displaced by the sulphones. The author, however, has continued to use it since 1951 and considers it to be more effective than the sulphones, particularly in cases of leprosy with neural involvement. His usual practice is to give thiacetazone in a dosage of 25 to 50 mg. orally three times a day; no toxic effects have been observed.

In 85 cases of the lepromatous type of leprosy good results were observed after 4 to 6 months, only one of the 85 patients showing no response. In 75 tuberculoid cases the results were satisfactory, improvement being observed in some cases within one month and marked regression of lesion in 6 months. In 3 out of 15 reactional tuberculoid cases striking amelioration was noted after only one month and in a further 8 by the end of 3 months, while in 35 indeterminate cases good results were noted after one month, the lesions clearing within one year. The drug had a satisfactory effect on the healing of nasal and other mucous membranes, while in several neural cases of more recent onset recovery of function was impressive. The author considers that

thiacetazone has about the same effect as the sulphones in clearing the tissues of bacilli. Histologically, it was observed that the cellular exudates were slow in clearing up. In 2 cases there was a change during treatment from the lepromatous to the reactional tuberculoid type of the disease. In tuberculoid cases the tuberculoid structure usually disappeared within 2 years, but a simple chronic type of cellular exudate may persist for longer than this. The author concludes that thiacetazone is not inferior to the sulphones in the treatment of all forms of leprosy, is particularly valuable in the neural type of the disease, is better tolerated than the sulphones, and in his experience has so far produced no toxic effects.

William Hughes

615. **Potentiating Effect of Quinolines on the Action of Tetracycline in Amoebic Dysentery**

S. J. POWELL, A. J. WILMOT, and R. ELSDON-DEW. *Lancet* [*Lancet*] **1**, 76–77, Jan. 9, 1960. 4 refs.

The tetracycline group of antibiotics are effective in acute intestinal amoebiasis, achieving cure in over 90% of cases. However, they have certain disadvantages—namely, they are expensive, relapses are common, and they do not prevent hepatic involvement. In this paper from the Amoebiasis Research Unit, Durban, South Africa, a trial is reported of small doses of tetracycline combined with quinolines in African males suffering from diarrhoea and ulceration as revealed by sigmoidoscopy, *Entamoeba histolytica* being present in the faeces. Varying combinations of the following treatment regimen were given: 50 mg. of tetracycline 3 times a day for 10 days, 600 mg. of diiodohydroxyquinoline 3 times a day for 20 days, and 800 mg. of chloroquine sulphate immediately, followed by 400 mg. 6 hours later, and then 200 mg. twice daily for 14 days.

After a period of 27 days from the start of treatment stools were negative for *E. histolytica* in 47 out of 50 patients treated with all three drugs, 15 out of 25 given tetracycline and diiodohydroxyquinoline, 12 out of 25 treated with tetracycline and chloroquine, and 5 out of 25 given diiodohydroxyquinoline and chloroquine. While a combination of tetracycline in a reduced dosage with quinolines was successful in eradicating *E. histolytica*, the ulcers healed more slowly than with larger doses of tetracycline.

[The experiments do not conclusively demonstrate potentiation, and the effect of the quinolines should be described as additive.] *R. A. Neal*

616. **Studies on Amebiasis. Part I—Amebiasis Past and Present**

J. R. SHAH, R. H. MEHTA, K. H. PATEL, and P. N. PHUTANE. *Indian Journal of Medical Sciences* [*Indian J. med. Sci.*] **14**, 84–91, Feb., 1960. 15 refs.

The authors first review previous work on the incidence of infection with *Entamoeba histolytica* in India, especially Bombay. They then describe their own results of a survey of bank employees and their families living in self-contained blocks of flats. A total of 473 adults were examined clinically and amoebiasis was diagnosed in 136 cases. On examination of the stools in these 136 cases *E. histolytica* was found in 81 instances, a second stool examination revealing a further 6 infections. This gives an incidence of 64%. The authors consider that comparison with the results of previous surveys shows a progressive increase in the frequency of amoebiasis.

[This paper is made confusing by the authors' incorrect use of the term amoebiasis, by which they presumably mean symptomatic infection with *E. histolytica* or amoebic dysentery. They have not determined the true incidence of this parasite, but only that in a selected series of cases.] *R. A. Neal*

617. **Studies on Amebiasis. Part II—Further Report on Treatment of Intestinal Amebiasis with Mebinol, a New Dichloracetamide Compound**

J. R. SHAH, R. H. MEHTA, K. H. PATEL, and P. N. PHUTANE. *Indian Journal of Medical Sciences* [*Indian J. med. Sci.*] **14**, 92–97, Feb., 1960. 15 refs.

The 87 cases of amoebic dysentery diagnosed clinically and parasitologically as described in the previous paper [see Abstract 616] were treated with "mebinol", a dichloracetamide compound of Italian origin. The drug was administered in doses of 500 mg. 3 times a day for 10 days [? by mouth]. After completion of treatment two stool examinations were made at an interval of 10 days and, in 26 cases, three further examinations at intervals of 4 to 5 weeks. Twenty days after treatment 72 subjects were free from *Entamoeba histolytica* (91% cure) and after 12 weeks 19 out of 26 (73%) were still free from the parasite. There were no serious side-effects.

[The 91% cure, according to a footnote to the table, includes the results of a second course of treatment. This is not mentioned elsewhere in the paper and it is therefore impossible to estimate the activity of mebinol.] *R. A. Neal*

618. **Studies on Amebiasis. Part III—Chemoprophylaxis in Amebiasis with Mebinol**

J. R. SHAH, R. H. MEHTA, K. H. PATEL, and P. N. PHUTANE. *Indian Journal of Medical Sciences* [*Indian J. med. Sci.*] **14**, 98–110, Feb. 1960. 2 figs., 27 refs.

Having studied the therapeutic activity of "mebinol" [see Abstract 617] the authors investigated its prophylactic effect. The patients cured by mebinol were divided into 2 groups; the first group, of 38 patients, were given 500 mg. of mebinol twice weekly [? by mouth], the second group, of 26 patients, remaining untreated as a control. Both groups were examined for the presence of *Entamoeba histolytica* in the stools 4 to 5 weeks, 10 weeks, and 14½ weeks after the start of the experiment. In the prophylactic group the numbers of positive results were 6, 2, and 0, while in the untreated group the numbers were 3, 8, and 9. A third group of patients whose stools were negative for *E. histolytica* were re-examined at the end of 24 weeks; during this period 4 patients (12%) had acquired an infection. *R. A. Neal*

619. **Newer Drugs in Amebiasis.** [Review Article]

H. H. ANDERSON. *Clinical Pharmacology and Therapeutics* [*Clin. Pharmacol. Ther.*] **1**, 78–86, Jan.–Feb., 1960. 31 refs.

Allergy

620. **Dominant and Recessive Precipitating and Desensitizing Haptens: Introductory Report**
O. Swineford Jr., S. Quelch, and D. Samsell. *Annals of Allergy* [*Ann. Allergy*] **18**, 276–280, March, 1960. 12 refs.

This preliminary report from the University of Virginia School of Medicine, Charlottesville, describes desensitization experiments in which 8 guinea-pigs were passively sensitized with Type-II antipneumococcal rabbit serum. Half the animals were then desensitized by giving 5 to 8·6 mg. of dextran in 5 or 6 intraperitoneal increments. When they were challenged several hours later with 5 mg. of dextran there was no reaction, but on challenge with 0·2 mg. of Type-II pneumococcal polysaccharide 2 of them died and the other 2 suffered from severe, though non-fatal, anaphylactic shock. The other 4 animals were desensitized by the intraperitoneal injection of 3 increments of Type-II pneumococcal polysaccharide; when challenged next day with both haptens there was no anaphylactic reaction to either the Type-II polysaccharide or to the dextran. (A control group of 4 sensitized guinea-pigs which had not been desensitized all died of acute anaphylactic shock on being similarly challenged.) The polysaccharide is therefore regarded as the dominant hapten and the dextran as the recessive hapten, since the former desensitized against both types of challenge. It is suggested that theoretically at least suitable haptens might be used for permanent desensitization, as they can neutralize sensitizing antibodies without eliciting more antibody formation anamnestically.

H. Herxheimer

621. **Choline Theophyllinate in Children with Asthma: a Controlled Trial**
L. B. Strang and E. G. Knox. *Lancet* [*Lancet*] **1**, 260–262, Jan. 30, 1960. 8 refs.

A double-blind controlled trial of choline theophyllinate in the treatment of chronic asthma in 14 children aged 7 to 13 years is reported in this paper from the Department of Child Health, King's College, University of Durham. The forced expiratory volume in 1 second ($F.E.V._1$) provided a satisfactory indication of respiratory function. The children were given either 200 mg. of choline theophyllinate 4 times a day or a lactose tablet at similar intervals. After 3 months the medicaments were reversed for a similar period. The patients were seen at 14-day intervals.

On the basis of the views of the patients themselves and of the number of attacks of asthma that occurred between each visit there did not appear to be any significant difference between the two treatments. Physical signs were not significantly different in the two groups. However, comparison of the $F.E.V._1$ expressed as a percentage of the normal for height did show an appreciable difference between the two treatments, the mean performance being better with choline theophyllinate than with lactose in 10 of the 14 children. These differences were independent of the order in which the drugs were given. The authors consider, however, that the benefit achieved was small.

[This investigation confirms that choline theophyllinate by mouth has some bronchodilator activity when compared with a placebo, but it also indicates that the value of the drug as a symptomatic remedy is slight.]

R. S. Bruce Pearson

622. **Dexamethasone in Childhood Asthma**
C. J. Falliers and S. C. Bukantz. *Annals of Allergy* [*Ann. Allergy*] **17**, 887–894, Nov.–Dec., 1959 [received Feb., 1960]. 11 figs., 4 refs.

Dexamethasone was substituted for prednisone in the treatment of 21 children between the ages of 6 and 13 years admitted to the Jewish National Home for Asthmatic Children, Denver, Colorado, suffering from intractable asthma. For all but the most severe cases 2·5 to 10 mg. of prednisone a day had proved to be a sufficient maintenance dose. About 0·75 mg. of dexamethasone was substituted for each 5 mg. of prednisone, and it was found that severe side-effects such as moonface, hirsutism, and striae did not occur unless a daily dose of 1·5 mg. of dexamethasone was exceeded. An attempt to determine the maintenance dose of this drug individually by trial and error was not made, but it is estimated that, weight for weight, dexamethasone is about 6 times more effective than prednisone. *H. Herxheimer*

623. **Prolonged Prophylaxis of Asthma in Childhood with Sulfamethoxypyridazine (Kynex).** [In English]
E. Ryssing. *Acta allergologica* [*Acta allerg.* (*Kbh.*)] **15**, 53–60, 1960. 1 fig., 19 refs.

Since infections of the upper respiratory tract often provoke asthmatic symptoms in asthmatic children, long-term prophylaxis with penicillin, the tetracyclines, or sulphonamides has been tried by a number of workers. Evaluation is difficult, and this in uncontrolled trials probably accounts for the differing results. At the Municipal Out-patient Clinic for Allergic Diseases in Children, Copenhagen, the author tried long-term prophylaxis with sulphamethoxypyridazine, a double-blind technique being used. This sulphonamide is rapidly absorbed and slowly eliminated, so that a single daily dose is sufficient to achieve an effective plasma concentration. The trial was conducted over the period September, 1958, to March, 1959. Analysis of the results showed that sulphamethoxypyridazine has no effect on the frequency of asthmatic attacks, and is therefore not indicated in the treatment of asthma in childhood.

A. W. Frankland

Nutrition and Metabolism

624. **Fat Emulsions for Clinical Intravenous Therapy**
E. H. STORER. *A.M.A. Archives of Surgery* [*A.M.A. Arch. Surg.*] **80**, 214–218, Feb., 1960. 2 figs., 12 refs.

Fat emulsions for intravenous administration are usually prepared by homogenizing about 10% fat in a watery solution of 5% glucose and/or protein hydrolysate. Since these emulsions deteriorate in storage, apparently by hydrolysis, the author, working at the University of Tennessee College of Medicine, has tried an anhydrous emulsion which stands autoclaving and consists of an oil, an emulsifying agent, and glycerol, with a fat particle size of less than 2 μ. The emulsion is diluted with a 5% glucose and/or a 5% protein hydrolysate solution in water just before use; the emulsion then contains 10% of safflower oil, 0·5% of phosphatide, and 8% of glycerol. A total of 826 infusions of this preparation have been given for periods up to 2 months. The overall reaction rate, including side-effects, was 13·6%. The more serious side-effects occurred after extensive administration and were apparently caused by the overloading of the reticulo-endothelial system with fat. Symptoms of early reaction, which were transient, included back pain, malaise, fever, restlessness, and anaemia.

H. E. Magee

625. **Vitamin-A Deficiency following Total Gastrectomy**
J. F. ADAMS, J. M. JOHNSTONE, and R. D. HUNTER. *Lancet* [*Lancet*] **1**, 415–417, Feb. 20, 1960. 20 refs.

In this paper from the Western Infirmary, Glasgow, and the Vale of Leven Hospital, Alexandria, 5 cases of vitamin-A deficiency following total gastrectomy are reported.

In all the patients the fasting serum vitamin-A level was subnormal; the peak values after administration of vitamin A were lower than those in healthy subjects. However, after treatment with vitamin A for 2 to 3 weeks the post-absorption serum levels were normal. There was poor dark adaptation in 4 patients who, however, had not noticed night blindness; the patient with normal dark adaptation had follicular keratitis. Absorption of fat was much impaired in 3 patients and slightly below normal in 2. Jejunal biopsy specimens were normal.

The authors state that the cause of the deficiency in these patients, all of whom had an " adequate " dietary intake, is obscure; in only one patient could it be attributed to the steatorrhoea. They were impressed with the rapid transit time of a barium bolus and suggest that as a result there may be only limited time for the mixing of food with pancreatic enzymes and hence impaired absorption. Although the deficiencies of vitamin A were not gross enough to produce keratomalacia, the authors consider that such deficiencies can only be detrimental to health. They recommend that patients who have undergone total gastrectomy should be given a 2-week course every 6 months of vitamin A by mouth in a daily dosage of 100,000 units.

A. Gordon Beckett

626. **The Metabolism of Strontium in Children**
J. BEDFORD, G. E. HARRISON, W. H. A. RAYMOND, and A. SUTTON. *British Medical Journal* [*Brit. med. J.*] **1**, 589–592, Feb. 27, 1960. 19 refs.

The daily urinary and faecal excretion of strontium and calcium for 4 children between the ages of 4¾ and 14½ years has been measured over an initial period of 7 or 8 consecutive days immediately before an oral dose of about 100 mg. of strontium (as strontium chloride) taken at breakfast-time. Subsequently, the daily urine and faecal excretion of strontium and calcium was estimated over a period of from 12 to 18 days and the net retention of the dose deduced. The results are compared with the excretion of an oral dose of strontium by adults.

The mean, cumulative, urinary excretion of a single oral dose of strontium was about 3% for the children up to 16 days after the dose, with the exception of a boy 14½ years old. The corresponding faecal excretion was about 78% of the dose. The respective excretions, over a similar period, for adults were 19% and 64% of the dose. Thus the retention (dose−excretion) up to 16 days after the dose was not significantly different in the two age-groups.

An attempt made to compare values derived for the overall discrimination of strontium relative to calcium in children and adults tends to show that it is rather higher in children.—[From the authors' summary.]

627. **The Digestion and Absorption of Protein by Normal Man**
C. W. CRANE and A. NEUBERGER. *Biochemical Journal* [*Biochem. J.*] **74**, 313–323, 1960. 4 figs., 40 refs.

Although protein metabolism has been widely investigated in the past 50 years, there is still uncertainty regarding the nature of the products of digestion and the time required for enzymic hydrolysis and actual absorption. It was thought that radioactive nitrogen (^{15}N) might be of value in elucidating these points.

In the study here reported from St. Mary's Hospital Medical School, London, healthy human subjects aged 30 to 40 years were given yeast protein or yeast protein hydrolysate labelled with ^{15}N in amounts equivalent to 0·4 to 0·9 mg. of ^{15}N per kg. body weight. Urine, blood, and faeces were collected at intervals and the content of ^{15}N in various fractious was determined. It was found that the rate of absorption of whole yeast protein was very similar to that of the protein hydrolysate, although some slight—and probably significant—differences were noted. A significant amount of absorption appeared to

occur within 15 to 20 minutes of ingestion. The rate of absorption was at a maximum at about 45 minutes and was largely completed in 75 to 90 minutes. The significance of these findings is discussed in relation to current theories about the digestion and absorption of proteins. *H. Harris*

628. **Anterior Pituitary Deficiency in Disorders Associated with Steatorrhoea**
J. N. MICKERSON. *British Medical Journal* [*Brit. med. J.*] **1**, 529–534, Feb. 20, 1960. 2 figs., 46 refs.

The author has investigated, at Charing Cross Hospital, London, the endocrine system of 7 female patients aged between 16 and 64 years who were suffering from steatorrhoea. Pigmentation of the skin, reminiscent of Addison's disease, was present in 5 patients, 3 of whom also had buccal pigmentation, while in 3 the axillary hair was absent and the pubic hair was sparse. In all 7 patients the urinary excretion of 17-ketosteroids was subnormal, but increased when ACTH (corticotrophin) was given. Administration of this hormone also caused a decrease in the number of circulating eosinophils. Performance of the first part of the Robinson–Power–Kepler test on 5 of the patients showed that in all 5 the volume of "day urine" (that is, the largest hourly specimen of those collected between 9.30 a.m. and 12.30 p.m. after a water load of 20 ml. per kg. body weight given at 8.30 a.m.) failed to exceed that of the "night urine" (that is, all urine excreted between 10.30 p.m. and 7.30 a.m.). Tests with radioactive iodine on 2 patients showed subnormal thyroid activity in one and a low normal activity in the other.

The author concludes that the findings provide evidence of anterior pituitary deficiency in these patients and he attributes the beneficial effects of steroid therapy in steatorrhoea to the correction of the resulting secondary adrenocortical deficiency. *Charles Rolland*

629. **Hypocholesteremic Effect of Benzmalacene**
I. H. PAGE and R. E. SCHNECKLOTH. *Circulation* [*Circulation*] **20**, 1075–1078, Dec., 1959. 1 fig., 4 refs.

Probenecid inhibits the acetate activation of coenzyme A and it also interferes slightly with hepatic synthesis of cholesterol; in this way it indirectly lowers the serum cholesterol level. Benzmalacene has a quite different chemical nature, but it is much more active than probenecid in inhibiting the incorporation of acetate and mevalonic acid into the synthesis of cholesterol *in vitro*; in dogs it interferes with cholesterol synthesis and sharply reduces the serum cholesterol level.

In investigations reported from the Cleveland Clinic Foundation, Cleveland, Ohio, 250 mg. of benzmalacene was given 2 to 4 times a day to 19 patients (13 men, 6 women), 12 of whom were hypertensive, while the other 7 exhibited hyperlipaemia and hypercholesterolaemia. The serum cholesterol level was reduced considerably in all but 2 hypertensive and 3 hypercholesterolaemic patients after one month, and the reduced cholesterol level was maintained in most cases for 4 months. In 2 hypercholesterolaemic patients in whom there was a significant reduction of the serum cholesterol level a sharp rise in the serum triglyceride level occurred, while the cholesterol:phospholipid ratio fell and the free:total cholesterol ratio rose. Liver function, as measured with "bromsulphalein" after 4 months' administration of benzmalacene, had deteriorated in 8 of the 12 patients investigated. Nausea, diarrhoea, and epigastric discomfort occasionally required discontinuation of the administration of the drug.

The authors suggest that drugs which interfere with cholesterol synthesis "should be carefully studied in animals for long periods and in a few select patients before they are used in the hopes of preventing atherosclerosis".

[It has still to be proved by direct evidence that there is a positive correlation between hypercholesterolaemia and atherosclerosis in man.] *Z. A. Leitner*

630. **Treatment of Wilson's Disease with Penicillamine**
J. M. WALSHE. *Lancet* [*Lancet*] **1**, 188–192, Jan. 23, 1960. 4 figs., 18 refs.

Up to 1948 it was generally considered that there was no satisfactory treatment for Wilson's disease in which copper is deposited in various organs, chiefly the brain, liver, and kidneys, with the result that degenerative changes subsequently develop in these organs. In that year it was shown that dimercaprol (BAL) had a real if limited action in removing copper from the tissues. Since then a number of other agents have been tried, of which the latest is penicillamine ($\beta\beta$-dimethyl cysteine). The author has gathered together data from four different countries regarding 22 cases of the disease (18 from the British Isles, 2 from Canada, and one each from Germany and Israel) which had been treated with penicillamine, the daily dose varying from 0·5 to 3 g. per day. In most cases the drug was given in short courses of 5 days every 10 days or at monthly intervals, the duration of treatment varying widely from 4 weeks to 3 years. Dimercaprol was also given in 16 cases, either alone or in combination with penicillamine, the former being administered in short courses each of 5 to 7 days in a dosage of up to 400 mg. daily.

Under treatment with penicillamine 6 patients became symptom-free, 11 showed a good if limited response, and 3 showed no response; the other 2, who had biochemical stigmata of the disease, had received penicillamine prophylactically and in these no neurological symptoms developed. Side-effects of the drug included mild transitory rashes in 2 patients, one of whom also developed Jacksonian epilepsy under this treatment. The author concludes that penicillamine is of value in Wilson's disease and is more active than dimercaprol in mobilizing copper and promoting clinical well-being. The rate of response to penicillamine is slower than that to dimercaprol, but on the other hand the improvement is better maintained and is often continuous over a period of years. Unfortunately the type of patient who will respond is not known. There is no correlation between the biochemical and the clinical findings, and the latter give no guide to prognosis. The mechanism of action of the drug and the reasons for biochemical resistance to it in some cases remain to be determined.

Norval Taylor

Gastroenterology

631. **Peptic Ulcer: Treatment with Antacids and a Mucin-like Substance**
J. A. RIESE. *American Journal of Gastroenterology* [*Amer. J. Gastroent.*] **33**, 208–213, Feb., 1960. 2 figs., 8 refs.

At the Jersey City Medical Center, New Jersey, the effect on peptic ulceration of guar cellupectinoid, a plant mucin complex, was studied in a number [unspecified] of Shay rats and in 78 patients with peptic ulceration or hyperacidity due to hypertrophic gastritis. The drug was administered in tablets containing 275 mg. of the mucin complex, 70 mg. of magnesium oxide, 80 mg. of aluminium hydroxide, and 160 mg. of magnesium trisilicate. The number of tablets given to the rats is not stated, but only 22% had ulcers compared with 73% of untreated control animals. Of the 78 patients, 63 experienced adequate sustained relief. Initially 36 patients were given a control medication consisting of the antacids without the mucin; 10 did not benefit from this treatment. After an interval [unspecified] all 36 were given the tablets containing the mucin and in 33 symptoms were relieved. Gastroscopy in 4 patients showed the mucin-containing tablet still adhering to the gastric mucosa after 4 hours. A dosage of 2 tablets every 3 to 4 hours proved sufficient. There were no side-effects of the treatment. *R. Schneider*

632. **The Relation between Pain and Emptying of the Stomach in Duodenal Ulcer. Therapeutic Implications.** (Le rapport entre la douleur et l'évacuation de l'estomac dans l'ulcère duodénal. Ses conséquences thérapeutiques)
M. H. J. N. DEKKERS. *Archives des maladies de l'appareil digestif et des maladies de la nutrition* [*Arch. Mal. Appar. dig.*] **49**, 69–80, Jan.–Feb., 1960. 43 refs.

The author has investigated clinically and radiologically the rate of emptying of the stomach in 68 patients with proven duodenal ulcer after the ingestion of a meal consisting of bread, butter, cheese, and milk together with some barium. In the majority of patients the stomach was not empty until 5 or 6 hours (range 3 to 10 hours) after the meal; when pain occurred (29 cases) it did so during the period of emptying, usually between 2 and 4 hours after the meal, and ceased when the stomach was empty. The stomach contents were very acid when pain was present, and the author considers that acid secretion in response to the ingestion of food is the main cause of ulcer pain.

In view of these findings and also since carbohydrates do not undergo acid digestion in the stomach and do not stimulate acid secretion to the same extent as fats and protein the author has since 1953 treated 236 patients with duodenal ulcer with a daily diet consisting mainly of cereals, fruits, one or 2 eggs, a little butter (30 g.), and occasionally 50 g. of lean meat. In 216 (91·5%) of these patients ulcer pain disappeared in a few days, although rest in bed was not enforced. Of the 236 patients, 217 remained free of symptoms for 1½ to 4 years. The author admits, however, that the diet recommended is not very palatable and that long-term results are difficult to assess since many patients were tempted to depart from the regimen after some time. In his opinion the only alternative to a strict diet is subtotal gastrectomy, which was carried out in 40 cases, usually at the patient's request. *P. C. Reynell*

LIVER

633. **Renal Haemodynamics in Hepatic Cirrhosis**
K. H. ÖNEN. *Lancet* [*Lancet*] **1**, 203–204, Jan. 23, 1960. 9 refs.

Renal haemodynamics were studied in 17 cases of portal cirrhosis. In 12 progressive and severely decompensated cases haemodynamic figures were strikingly low. On the other hand, in 5 mild and regressive types of cirrhosis, glomerular filtration-rate and renal plasma flow were normal. Total urinary formaldehydogenic steroids were normal or slightly reduced in both groups. The possible role of renal haemodynamics in salt and water retention in cirrhosis are briefly discussed.—[Author's summary.]

634. **The Kidney as a Source of Blood Ammonia in Patients with Liver Disease: the Effect of Acetazolamide**
E. E. OWEN, M. P. TYOR, J. F. FLANAGAN, and J. N. BERRY. *Journal of Clinical Investigation* [*J. clin. Invest.*] **39**, 288–294, Feb., 1960. 34 refs.

The administration of the diuretic acetazolamide (" diamox ") to patients with liver disease is known to produce in some cases a rise in the arterial blood ammonia level and occasionally neuro-psychiatric deterioration. The authors, working at Duke University Medical Center and the Veterans Administration Hospital, Durham, N. Carolina, have studied the effect of this drug on the renal production of ammonia in 11 patients, of whom 9 were suffering from portal cirrhosis and 2 from fatty liver. By catheterizing the right renal vein they were able to compare the ammonia level in the renal vein with that in the arterial blood. The *p*H of the urine and blood, renal plasma flow, and renal oxygen consumption were also determined before and after the injection of 500 mg. of acetazolamide intravenously.

After the injection there was an abrupt and twofold increase in the ammonia concentration in the renal vein, followed later by a significant increase in the arterial blood ammonia level. There was an equally rapid decrease in urinary ammonia excretion and the urine became more alkaline. There was no change in renal blood flow during the period of the investigation,

but a significant decrease in the *p*H of the arterial blood and an increase in renal oxygen consumption were noted. It is concluded that these results indicate that there is increased production of ammonia in the kidneys following the administration of acetazolamide and that this accounts for the increased blood ammonia level and may be the cause of the neuro-psychiatric complications. The effect of acetazolamide in diminishing the uptake of ammonia in the peripheral tissues may also be of importance in increasing the blood level of ammonia, but the authors consider that the increased transfer of ammonia from the kidneys is of greater significance. Present evidence suggests that the excretion of ammonia into the urine may occur by a process of passive diffusion conditioned by the urinary *p*H, which influences not only the urinary ammonia excretion, but also the level in the renal vein. The increased urinary *p*H produced by acetazolamide results in a diminished urinary excretion of ammonia accompanied by its increased excretion into the blood stream via the renal veins. These observations therefore again demonstrate the possible importance of the sites of ammonia production, other than the alimentary tract, in the pathogenesis of hepatic coma.

A. E. Read

635. **Adrenocortical Steroid Metabolism and Adrenal Cortical Function in Liver Disease**

R. E. PETERSON. *Journal of Clinical Investigation* [*J. clin. Invest.*] **39**, 320–331, Feb., 1960. 3 figs., bibliography.

In the light of evidence that the liver plays an important part in the metabolism of adrenocortical steroids the author has carried out, at the National Institute of Arthritis and Metabolic Diseases, Bethesda, Maryland, an extensive study of the state of adrenocortical function in 14 patients with portal cirrhosis and 3 with acute viral hepatitis; in only one of the former group was the cirrhosis of non-alcoholic aetiology. The plasma levels of cortisol and corticosterone and the urinary excretion of the 17-ketosteroids, corticosteroids, and aldosterone were determined after the intravenous administration of 100 to 200 mg. of various adrenocortical steroids. By means of isotopic techniques the rates of disappearance of aldosterone and cortisol from the plasma were measured, and the size of the miscible pool of various steroids was estimated. The methods are briefly described.

The principal results obtained were as follows: (1) in all cases the plasma corticol level was normal and the corticosterone level low or just within the normal range; (2) the levels of urinary 17-ketosteroid and corticosteroid excretion were lower than normal in most of the patients; (3) after an infusion of cortisol (in 8 cases) this steroid disappeared from the plasma at a slower rate than normal; (4) a larger proportion of the infused cortisol appeared in the urine than occurs in normal subjects, but there was no apparent defect of conjugation of the 4 major metabolites of cortisol (infused in doses of 100 mg.); (5) the rate of cortisol secretion was shown to be lower than normal and this state of affairs also existed after the administration of ACTH. It is concluded from these studies therefore that there is no lack of cortisol in the plasma of the cirrhotic patient, but there would appear to be some defect in the utilization of this substance. This inability to metabolize cortisol normally was specific and was not seen with other steroids or their metabolites. The most likely explanation for the slower rate of metabolism of cortisol is thought to be an enzyme defect in the liver resulting in an impaired transformation of cortisol to its dihydro form. The faulty metabolism would also account for the larger proportion of infused cortisol appearing unchanged in the urine. The size of the miscible pool of cortisol and corticosterone was normal or nearly so. These patients with liver disease thus showed diminished adrenocortical function in that they produced less cortisol than normal subjects, but they compensated for this by slower utilization of the steroid, so maintaining a more or less normal plasma level. This is in contrast to the metabolism of the mineralo-corticoids, and in particular of aldosterone, which is produced in larger amounts than normal in some patients with liver disease, particularly in those with fluid retention.

A. E. Read

636. **I^{131}-Rose Bengal Test of Liver Function; a Clinical Evaluation**

A. M. GARCIA, K. AHMAD, A. V. WEGST, and W. H. BEIERWALTES. *Gastroenterology* [*Gastroenterology*] **37**, 725–734, Dec., 1959. 7 figs., 16 refs.

Rose bengal (tetraiodo-tetrachlorfluorescein) was used as early as 1923 in tests of liver function, but was later replaced by "bromsulphalein". However, the recent possibility of labelling rose bengal with radioactive iodine (^{131}I) and carrying out external counting over the liver area has reawakened interest in this test. At the University of Michigan Hospital, Ann Arbor, the authors have therefore sought to determine its clinical value by performing it on 26 control patients suffering from clinical disorders not associated with liver disease, on 43 unjaundiced patients with liver disease, and on 17 with obstructive jaundice. In all cases the bromsulphalein retention test was also carried out, with estimations of serum total, direct, and indirect bilirubin level, cephalin–cholesterol flocculation, thymol turbidity, serum alkaline-phosphatase level, serum transaminase activity, and serum albumin concentration. In 17 cases liver biopsy was also performed. The technique of the ^{131}I-rose bengal test, as modified by the authors, is described.

It was found that the test was less sensitive than the bromsulphalein excretion test in those patients with liver disease who were not jaundiced—in fact no difference was detected between unjaundiced patients with and those without liver disease. However, in the 17 patients with obstructive jaundice, 13 of whom were suffering from intrahepatic and 4 from extrahepatic obstruction, the technique, using combined head and abdominal counts, revealed good differentiation between these two sub-groups, but it is emphasized that the use of a head count alone, made after 40 minutes, failed to achieve this result. In all cases the diagnosis was confirmed by follow-up of the clinical course of the patient. In conclusion the authors present an original scheme of four combinations of curves for head and abdominal counts

which made it possible for them to differentiate diagnostically between various combinations of intrahepatic and extrahepatic obstruction. *J. Warwick Buckler*

637. **The Use of Prednisone to Initiate or Potentiate Diuresis in Chronic Hepatic Disease with Ascites**
J. V. CARBONE and H. B. MATTHEWS. *Gastroenterology* [*Gastroenterology*] **38**, 52–59, Jan., 1960. 6 figs., 38 refs.

The authors discuss the results obtained by the use of adrenal steroids in the treatment of patients with liver disease complicated by resistant ascites. At the San Francisco Hospital (University of California Service) 12 such patients were studied, 10 with portal cirrhosis, one with chronic viral hepatitis, and one with secondary biliary cirrhosis. The patients were confined to bed and were treated with a low sodium diet. They also received prednisone alone, chlorothiazide or meralluride alone, or a combination of one of these diuretics with prednisone. If diuresis did not occur all three agents were given. The dosage of prednisone was 20 or 40 mg. in four equal doses daily and that of chlorothiazide was 500 mg. four times daily. The mercurial diuretic was given by intramuscular injection in doses of 2 ml. at varying intervals. The body weight and urine volume were recorded daily, and 24-hour collections of urine were analysed for their content of electrolytes and nitrogen. Various liver function tests and biochemical investigations on the serum were performed.

Of 4 patients receiving prednisone alone, 2 had a brisk diuresis with loss of weight and ascites and a marked increase in urinary sodium excretion, while the other 2 had a mild diuresis and negligible weight loss. In 5 other cases neither prednisone alone nor one or other of the two diuretics alone produced a diuresis, but when the steroid was combined with chlorothiazide or meralluride a vigorous diuresis resulted in all of them. Three patients who proved refractory both to prednisone alone and to the combination of one of the diuretics with prednisone also failed to respond when both diuretics and prednisone were given together. The authors consider that the state of liver function did not affect the response to the drugs used, as evidence of a comparable degree of liver cell damage was present both in the patients who responded and those who remained refractory. Two patients treated with prednisone and chlorothiazide developed episodes of hepatic coma during this treatment.

This study is in agreement with other reports that prednisone may be of value in the treatment of fluid retention complicating liver disease. Prednisone could act either by increasing glomerular filtration or, as seems more likely, by inhibiting aldosterone or some other sodium-retaining hormone from acting on the renal tubule. Prednisone also has some action on water excretion, perhaps by inhibiting the production or action of the antidiuretic hormone. The precise mechanisms by which prednisone acts and potentiates the action of diuretics is unknown, but a trial of this therapy is worth while in patients with liver disease and resistant ascites.

[No mention is made of the aetiology of the cirrhosis in 10 of the 12 patients included in this study. If, as seems likely, they were alcoholics, cessation of drinking on admission could partly explain the good results obtained.] *A. E. Read*

638. **The Treatment of Ascitic Alcoholic Cirrhosis with Prednisone.** (Le traitement des cirrhoses ascitiques éthyliques par la Δ-cortisone)
M. P. VESIN. *Archives des maladies de l'appareil digestif et des maladies de la nutrition* [*Arch. Mal. Appar. dig.*] **48**, 1497–1532, Dec., 1959 [received Feb., 1960]. Bibliography.

This paper from the Hôpital Saint-Antoine, Paris, describes the results in 100 patients suffering from alcoholic cirrhosis of the liver, most of whom were treated with oral prednisone in the following dosage: 40 mg. on the first day, 30 mg. on the second day, 20 mg. on the third and following days, terminating with 10 mg. daily for a few days at the end of the treatment. The duration of treatment varied according to the results obtained, but was not longer than 25 to 30 days in favourable cases. The drug was administered even in grave cases, but never to patients in hepatic coma or to those with active gastro-duodenal ulcer, while the presence of azotaemic nephritis was also regarded as a contraindication. Other methods of treatment were withheld as far as possible during steroid therapy; the daily diet allowed contained 50 to 60 mEq. of sodium, and 1 to 2 g. of potassium chloride was given daily. In 44 cases the oedema disappeared completely during treatment and did not recur on its conclusion; in another 10 cases it cleared for a time, but recurred during treatment or soon afterwards, while in the remaining 46 cases the treatment had no effect on the oedema. In the 44 successful cases the clinical change was often most striking, beginning with subsidence of fever and being followed by sweating, considerable diuresis, and a markedly improved appetite.

The difficult problem of the mechanism by which prednisone reduces oedema is discussed. It might be expected that this drug, being a corticosteroid, would tend to cause sodium retention rather than the contrary. It is known, however, that sodium retention occurs when there is an excessive secretion of aldosterone by the adrenal glands. Moreover, some patients with oedema, irrespective of its cause, excrete excessive amounts of aldosterone in the urine. Determination of the urinary aldosterone excretion in some of the author's cases showed that this was abnormally high before the administration of prednisone, but these high levels returned to normal during administration of the steroid. In discussing these findings the author suggests that: (1) hypersecretion of aldosterone is the main mechanism causing sodium retention in these cases, although other mechanisms may also be involved; and (2) the action of prednisone in causing depletion of sodium is due to its effect in restoring the hypersecretion of aldosterone to normal levels. The data seem to indicate that prednisone also has a direct action in depleting the body of water. He concludes by pointing out that although this treatment is subject to the known disadvantages common to all forms of corticosteroid therapy in high dosage, there was no case of gastro-intestinal haemorrhage in this

series. Further, the treatment fails in many cases and even when successful it leaves the patient still liable to relapse. Nevertheless, it is considered to be a valuable, and perhaps the only, treatment for many of these cases.

Joseph Parness

639. **Hyperventilation and Arterial Hypoxemia in Cirrhosis of the Liver**

H. O. HEINEMANN, C. EMIRGIL, and J. P. MIJNSSEN. *American Journal of Medicine* [*Amer. J. Med.*] **28**, 239–246, Feb., 1960. 4 figs., 28 refs.

It has been shown that in patients with cirrhosis of the liver the plasma carbon dioxide level may be low as a result of chronic hyperventilation, but the mechanics of this hyperventilation are not known. The study reported in this paper from Francis Delafield Hospital and Columbia University, New York, was undertaken to determine the correlation between hyperventilation and hypoxaemia in cirrhosis. In 10 patients with cirrhosis of the liver and one with schistosomiasis a number of tests were carried out to obtain data on respiratory function, oxygen content and oxygen capacity of arterial blood, the CO_2 content and *p*H of the blood, oxygen diffusing capacity, and the arterial blood ammonia level.

It was found that in these cirrhotic patients hyperventilation, compensated alkalosis, and low arterial oxygen tension occurred concurrently. The low oxygen tension was best explained by some admixture of venous blood, conceivably via vascular communications which by-passed the alveolar capillary bed, probably through direct portal–pulmonary anastomoses. No explanation was forthcoming, however, for the associated hyperventilation.

John Fry

640. **Assessment of the Results of Surgical Treatment in Portal Hypertension**

A. I. S. MACPHERSON. *Gastroenterology* [*Gastroenterology*] **38**, 142–154, Feb., 1960. 7 figs., 21 refs.

The value of surgical treatment of portal hypertension has been assessed on the basis of the results obtained in 118 cases treated at Edinburgh Royal Infirmary, the majority being followed up over a period of 30 years. In 22 cases the obstruction was considered to be extrahepatic in origin. In 46 of the 96 cases of intrahepatic disease no aetiological factor could be found; in 25 the obstruction was attributed to post-necrotic cirrhosis and in 9 only to alcohol. From the results of a variety of tests carried out on 65 of the patients with cirrhosis the condition was classified as mild in 31, moderate in 21, and severe in 13. The prognosis appeared to depend more on the severity of the liver disease than on the age of the patient.

The author discusses the difficulties encountered in comparing the results of medical and surgical treatment of portal hypertension, but the comparative data available indicated that surgical treatment improved the prognosis only as regards survival in the first year. Operative treatment was followed immediately by deterioration in liver function, due in part to diversion of the portal blood. The condition of the liver initially was the main factor in determining the subsequent course of the cirrhosis. Shunt operations did not affect hypersplenism, and splenectomy was necessary to correct this.

The number of haemorrhages in patients treated surgically fell dramatically during the year following operation, but subsequently tended to rise. Early recurrence of haemorrhage was commonest in patients with the most severe liver disease; under 50% of these were alive a year after operation. Active haemorrhage from oesophageal varices was treated very conservatively by rest, sedation, and, if necessary, blood transfusion. Balloon tamponade was used only 5 times in the patients with cirrhosis and operation to control the haemorrhage was undertaken in only 3.

Haemorrhage was considered to be a direct or contributory cause of death in only 3 out of 65 patients with cirrhosis and 12 with extrahepatic block (175 episodes of bleeding).

B. F. Swynnerton

INTESTINES

641. **Toxic Dilation of the Colon in the Course of Ulcerative Colitis**

R. H. MARSHAK, B. I. KORELITZ, S. H. KLEIN, B. S. WOLF, and H. D. JANOWITZ. *Gastroenterology* [*Gastroenterology*] **38**, 165–180, Feb., 1960. 5 figs., 6 refs.

Acute colonic dilatation was observed on 19 occasions in 16 patients with ulcerative colitis admitted to the Mount Sinai Hospital, New York. On 4 occasions the dilatation occurred in ulcerative colitis of " fulminating onset ", on 14 during an acute exacerbation of the relapsing type of the disease, and on one occasion in a patient with continuous chronic disease.

All the patients were febrile, toxic, and dehydrated, and most of them had tachycardia, anaemia, and low blood pressure. Abdominal distension and tenderness, together with rebound tenderness, were present in 7 patients. The abdomen was often soft or doughy rather than rigid, and bowel sounds were usually decreased or absent. Moderate or severe rectal haemorrhage was a feature in some cases. Perforation was confirmed in 4 patients and suspected clinically in 9. A moderate leucocytosis was present in all except 3 of the cases. The serum chloride, sodium, and albumin values were usually below the normal; hypopotassaemia was not observed.

At first treatment was conservative, with intravenous infusions, administration of antibiotics, and, in 7 cases, " long tube intubation ". Of the 16 patients, 5 improved, but 2 subsequently relapsed and required colectomy. Of the remaining 11 patients, 2 died while receiving medical treatment, 6 were subjected to subtotal colectomy and ileostomy (one died), and 3 responded to caecostomy. Discussing the advantages and disadvantages of ACTH (corticotrophin) and steroids in the treatment of this condition the authors state that steroids should be avoided if there is coincident perforation, but that dramatic improvement may occur in the absence of perforation. They should also be avoided if the patient is known to have deep undermining ulcers in the large bowel.

B. F. Swynnerton

642. **Treatment of Ulcerative Colitis with a Resion Polymyxin Phthalylsulfacetamide Preparation**
R. EHRLICH. *American Journal of Gastroenterology* [*Amer. J. Gastroent.*] **33**, 235–239, Feb., 1960. 12 refs.

A compound consisting of an adsorbent mixture (a polyamine exchange resin, sodium aluminium silicate, and magnesium aluminium silicate) together with polymyxin B and phthalylsulphacetamide was tried in the treatment of 22 cases of ulcerative colitis. The adsorbent mixture is reputed to remove toxic material from the intestine and to inhibit lysozyme. The preparation was given in a dosage of 1 to 2 tablespoonfuls (15 to 31 g.) 4 times a day until the ulcerative process was resolved, or for 4 weeks if no improvement occurred. The criteria of improvement were based on the endoscopic and radiological appearances of the intestine. Of the 24 patients, 17 had complete remission of symptoms for 4 months to more than one year and 3 were improved. The remaining 4 patients did not benefit and were treated surgically. None of a group of 5 control patients given a placebo for 4 weeks showed any subjective or sigmoidoscopic improvement. *R. Schneider*

643. **Faecal Loss of Fluid, Electrolytes, and Nitrogen in Colitis Before and After Ileostomy**
F. G. SMIDDY, S. D. GREGORY, I. B. SMITH, and J. C. GOLIGHER. *Lancet* [*Lancet*] **1**, 14–19, Jan. 2, 1960. 9 figs., 9 refs.

At the General Infirmary at Leeds the loss of fluid, sodium, potassium, and nitrogen in the faeces was studied in 9 patients awaiting operation for ulcerative colitis, in 16 patients soon after proctocolectomy and ileostomy, and in 2 patients in whom an ileostomy had been established for about a year.

In all but 2 of the 9 patients studied before operation the maximum faecal volume exceeded the normal maximum of 400 ml. a day. In this group sodium loss in the faeces varied between 9 and 170 (normal 2 to 5) mEq. a day, while potassium excretion was also increased, though by not more than 2 or 3 times the normal (12 mEq. a day), except in one patient who lost 90 to 167 mEq. a day although his serum potassium level was normal [but this does not exclude potassium deficiency]. Faecal electrolyte loss was mainly related to faecal volume—more so for sodium than potassium. Fluid volume and sodium excretion rose when sodium was given by mouth. Nitrogen excretion exceeded 2 g. a day in the 7 patients in whom it was determined.

Of the 16 patients studied after operation, 11 were not given steroid therapy. In 2 of these the ileostomy started to work on the day of operation, in 4 on the first postoperative day, and in 5 on the second day. The volume of ileostomy fluid rose to a maximum (usually below 1,500 ml.) on the 3rd to 5th day and fell to 200 to 500 ml. by the end of the first week. By the 10th day the consistency of the ileostomy fluid resembled that of an established ileostomy. Sodium excretion fell from a high initial level (not above 130 mEq. a day) to 40 to 60 mEq. a day. Its concentration was fairly constant at about 120 mEq. per litre. Potassium loss was 1 to 12 mEq. a day, its concentration being variable. Nitrogen excretion was normal (0·4 to 1·8 g. daily). In the other 5 patients, who were given cortisone, the ileostomy started to work on the 3rd postoperative day, the output volume rising steadily to about 200 to 500 ml. daily. Sodium loss was smaller than in the group not given cortisone (less than 50 mEq. a day) and its concentration was about 109 mEq. per litre. Potassium excretion was 3 to 9 mEq. and nitrogen excretion 0·5 to 1·7 g. a day. In one patient who developed peritonitis the volume of ileostomy fluid rose considerably and sodium loss reached 300 mEq. and potassium loss 60 mEq. a day. In the 2 patients with established ileostomies fluid volume was 300 to 500 ml., sodium concentration being about 120 mEq. per litre. Potassium excretion was 3 to 4·8 mEq. and nitrogen excretion 0·5 to 2 g. a day.

The authors recommend that in the postoperative management of uncomplicated cases of ulcerative colitis the sodium lost through the ileostomy should be accurately replaced with normal saline (156 mEq. per litre) given intravenously. Potassium replacement is not necessary. *M. Lubran*

644. **Systemic and Local Corticosteroid Therapy in Ulcerative Colitis**
S. C. TRUELOVE. *British Medical Journal* [*Brit. med. J.*] **1**, 464–467, Feb. 13, 1960. 1 fig., 13 refs.

This paper from the Radcliffe Infirmary, Oxford, presents further observations on the use of corticosteroids in ulcerative colitis, planned to compare their relative efficacy when given by mouth and locally by rectal drip instillation. Patients were chosen who showed sigmoidoscopic evidence of ulcerative colitis of moderate or mild severity, those with severe disease and those suffering from haemorrhagic proctitis being excluded. The 120 patients were allotted at random to three groups which were treated as follows: (1) 5 mg. of prednisolone 4 times a day by mouth (40 patients); (2) nightly administration by rectal drip of 100 mg. of hydrocortisone hemisuccinate (20 patients) or 40 mg. of prednisolone 21-phosphate (20 patients); and (3) both treatments combined (20 patients receiving hydrocortisone and 20 prednisolone per rectum).

In Group 1 about one-third of the patients were in clinical remission at the end of the 2-week trial period. In Group 2 about three-quarters responded, and the response was approximately the same whether prednisolone 21-phosphate or hydrocortisone hemisuccinate was used. Comparison of these results shows clearly that greater benefit was derived from local than from oral administration of corticoids. When oral and local treatment were combined (Group 3) there was a further and statistically significant improvement in results. One marked advantage of local over systemic use of corticoids is that side-effects do not appear to arise.

[Clearly, neither the mode of action of corticosteroids nor the ideal dosage and duration of treatment is as yet fully understood. However, this paper provides further evidence of their therapeutic value in moderate cases, especially when given early, and the author is to be congratulated on a useful addition to the available means of treating ulcerative colitis.] *Thomas Hunt*

Cardiovascular System

645. **A Study of Etiologic Factors in So-called Primary Pulmonary Hypertension**
A. J. RAWSON and H. M. WOSKE. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **105**, 233–243, Feb., 1960. 7 figs., 32 refs.

The clinical and necropsy records of 4 cases of so-called primary pulmonary hypertension (P.P.H.) were studied at the University of Pennsylvania School of Medicine, Philadelphia. P.P.H. is defined as hypertension of the lesser circulation in the absence of heart disease (other than cor pulmonale), parenchymal lung disease, or vascular disease of known aetiology involving the pulmonary arterial tree. The histological appearances of the lungs were similar in all 4 cases, consisting essentially of marked intimal cellular proliferation in the small muscular arteries and arterioles with severe vascular stenosis. There was no evidence of repeated thrombo-embolism, which some workers have suggested as a possible aetiological factor in P.P.H. Arthritis and Raynaud's phenomena were present in 2 cases and extra-pulmonary lesions suggestive of a collagen disease in one. There was a history of arthritis and Raynaud's phenomena in the relatives of 2 patients.

A review of 39 well-documented cases reported in the literature revealed a higher than normal incidence of arthritis (8%), Raynaud's phenomena (21%), and lesions suggestive of collagen disease (10%) in patients with P.P.H. It is suggested that in many if not in most cases of P.P.H. the condition may be related to the collagen group of diseases. *A. J. Karlish*

646. **The Influence of Phenobarbitone on Functional Electrocardiographic Changes.** (Funkční elektrokardiografické změny a jejich ovlivnění fenobarbitalem)
J. KOŤÁTKO. *Časopis lékařů českých* [*Čas. Lék. čes.*] **99**, 221–224, Feb. 19, 1960. 2 figs., 8 refs.

Many abnormal electrocardiograms (ECGs) have no pathological anatomical basis, because the abnormality is of a nervous character. Nordenfelt has demonstrated that such cases may be distinguished by means of ergotamine which, through its action on the sympathetic system, restores the ECG to normal. The author of the present article, however, is of the opinion that changes in the central nervous system are much more responsible for nervous disturbances in the ECG than increased sympathetic tone.

In experiments on 20 subjects with a normal heart and 20 patients with cardiac disturbances of nervous origin it was shown that phenobarbitone in normal or high doses can influence the normal ECG and can remove abnormalities due to nervous disorders. The advantage of using phenobarbitone for this purpose rather than ergotamine lies in its absence of side-effects. It is emphasized, however, that a positive effect of phenobarbitone on the ECG does not always exclude an organic basis for the disturbances. Similarly a nervous origin cannot be excluded entirely in cases in which an abnormal ECG is influenced only slightly or not at all by phenobarbitone. *M. Hrusak*

647. **Ventricular Septal Defect. I. Congestive Heart Failure in Infancy**
B. C. MORGAN, S. P. GRIFFITHS, and S. BLUMENTHAL. *Pediatrics* [*Pediatrics*] **25**, 54–62, Jan., 1960. 3 figs., 22 refs.

The authors of this paper from the Babies Hospital and the College of Physicians and Surgeons, Columbia University, New York, trace the clinical course of 17 infants with ventricular septal defects who developed congestive cardiac failure during the first year of life. In all cases the initial episode of decompensation occurred when the infant was one to 6 months of age. In 10 of the 17 the heart failure persisted and the child died before the age of one year. The remaining 7 patients were still alive at the time of the report [but the follow-up period of some of these is only one or two years].

Comparison of the clinical, electrocardiographic, and radiological findings did not reveal any differences between the children who died and those who survived. Signs of congestive failure in both groups were predominantly right-sided, and all the patients received digitalis. Cardiac catheterization was carried out in 8 cases (including one which was subsequently fatal); moderate or severe pulmonary hypertension was found. In the fatal case severe pulmonary hypertension was present, but the findings on catheterization differed little from those of another child who survived.

The authors conclude that in infants with cardiac failure due to a ventricular septal defect there is at present no known method of determining who will survive and who will die; the crucial time is the first year of life. Exacerbations after the first year are rare.
John Rendle-Short

648. **Postpericardiotomy Syndrome following Penetrating Stab Wounds of the Chest: Comparison with the Post-commissurotomy Syndrome**
F. SEGAL and B. TABATZNIK. *American Heart Journal* [*Amer. Heart J.*] **59**, 175–183, Feb., 1960. 4 figs., 27 refs.

The authors describe 2 cases admitted to Baragwanath Hospital, Johannesburg, in which the postpericardiotomy syndrome developed after penetrating stab wounds of the chest. The clinical features of the syndrome, which occurred 3 months and 3 weeks respectively after the initial injury, were identical with those of the so-called post-commissurotomy syndrome and included pyrexia and pericarditis with spontaneous recovery. The condition is thought to be due to blood in the pericardial cavity causing a traumatic pericarditis. *R. L. Hurt*

649. **Ventricular Fibrillation: Treatment and Prevention by External Electric Currents**
P. M. ZOLL, A. J. LINENTHAL, and L. R. N. ZARSKY. *New England Journal of Medicine* [*New Engl. J. Med.*] **262**, 105–112, Jan. 21, 1960. 4 figs., 16 refs.

In a previous paper (*New Engl. J. Med.*, 1956, **254**, 727; *Abstr. Wld Med.*, 1956, **20**, 282) the authors described their technique for the treatment and prevention of ventricular fibrillation by the application of external electric countershock. In the present paper from Beth Israel Hospital and Harvard Medical School, Boston, they describe further experience with this method, in which an alternating current (60 cycles, 0·15 second, 150 to 450 volts) is applied to the unopened chest with large electrodes. They have used the electric defibrillator in the treatment of 8 patients with atrioventricular block who were suffering from attacks of ventricular fibrillation or tachycardia. In attacks of unconsciousness due to cardiac standstill electric countershock produced a return to idioventricular rhythm with recovery of consciousness. The treatment must be carried out within 4 minutes of the onset of the attack. It follows that cardiac monitoring, which provides immediate recognition of cardiac arrest and identification of the arrhythmia, is required. Of the 8 patients, 5 died 19 hours to 4 months later and only one survived as long as 2½ years after the initial countershock. *A. I. Suchett-Kaye*

MYOCARDIAL INFARCTION AND CORONARY DISEASE

650. **The Anoxia Test for Myocardial Ischaemia**
N. COULSHED. *British Heart Journal* [*Brit. Heart J.*] **22**, 79–93, Jan., 1960. 10 figs., bibliography.

In this paper from the Regional Cardiac Centre, Sefton General Hospital, Liverpool, the author describes the results obtained in a large series of patients with Malmstrom's modification of the Levy anoxia test for the detection of myocardial ischaemia, in which a gas mixture consisting of 6·5% oxygen and 4·5% carbon dioxide in 89% nitrogen is delivered to the patient through a standard anaesthetic face-piece, rebreathing being prevented. The 111 patients studied had received no vasodilator drugs for the preceding 12 hours and the test was always carried out following a period of rest and at least 2 hours after a meal. Full 12-lead electrocardiograms were recorded by a direct-writing machine and the interpretation of the tracings was based upon Levy's work, a total of 126 tests being carried out. The patients were divided into four groups as follows: (1) 41 patients with no clinical evidence of organic cardiovascular disease; (2) 53 in whom coronary arterial insufficiency was suspected on clinical grounds, these being subdivided into (*a*) 10 in whom coronary arterial disease was known to exist, (*b*) 10 who had no history of myocardial infarction, but in whom the resting electrocardiogram (ECG) was abnormal, (*c*) 14 with normal or only slightly abnormal ECGs at rest, but with a clinical history suggestive of angina pectoris, although other possible sources of pain were present, and (*d*) 19 patients similar to those in Subgroup (*c*) except that no alternative source of pain was apparent; (3) 7 patients with peripheral arterial disease and intermittent claudication, but no angina pectoris, and (4) a miscellaneous group of 10 patients of whom 5 had diaphragmatic hernia and 2 suffered from fainting attacks.

In Group 1 the results of the anoxia test were negative in all cases. In Group 2 (*a*) 8 tests produced 6 positive results, in Group 2 (*b*) all results were positive, in Group 2 (*c*) the result was positive in 12 of 13 cases in which it was performed, and in Group 2 (*d*) 16 of 18 tests completed gave a positive result. It was in Group 2 (*c*) that the test was of special value, since it established the presence of coronary insufficiency in 12 patients in whom the disability was suspected, but had not been confirmed by previous methods of examination. The test gave positive results in 3 of 5 patients in Group 3 with intermittent claudication but no chest pain, and also in 3 patients belonging to Group 2 who had intermittent claudication as well as angina pectoris; it is pointed out that in these cases the anoxia test was particularly useful because of the patients' inability to carry out an exercise test. In Group 4 results were negative in all 5 patients suffering from diaphragmatic hernia, but it is of interest that in 4 patients in Group 2 also with radiologically proven diaphragmatic hernia, but with symptoms suggesting angina pectoris, the result was positive, thus supporting the clinical impression that such hernia alone does not produce anginal pain; of the 2 patients in Group 4 suffering from fainting attacks, one showed a positive result and was probably suffering from Stokes–Adams syncope, but in the other, in whom the condition was thought clinically to be non-organic in nature, the result was negative.

It is concluded that although the anoxia test is more time-consuming than the exercise test, it is safe, simple to perform, and has the advantage over the latter in that the patient is not only under continuous ECG observation, but has immediately available a supply of oxygen. As noted it is of especial value in patients who are incapable of exertion. It is pointed out, however, that the test should be regarded as mainly an adjuvant to careful clinical assessment and routine electrocardiography.
J. Warwick Buckler

651. **Lipoproteins, Cholesterol and Serum Proteins as Predictors of Myocardial Infarction**
I. H. PAGE and L. A. LEWIS. *Circulation* [*Circulation*] **20**, 1011–1027, Dec., 1959. 2 figs., bibliography.

The problem of the relationship of the serum cholesterol level and lipoprotein fractions to the occurrence of coronary atherosclerosis and myocardial infarction is still unsettled. Although it has been repeatedly found that the serum lipoprotein pattern of normal persons measured by ultracentrifugation at a specific gravity of 1·063 (Gofman's method) varies relatively little, variations in the pattern are revealed when the density is raised to 1·21 with potassium bromide (Page's modification).

On examining the blood of 6 normal women weekly for 5 months the present authors, working at the Cleveland Clinic Foundation, Cleveland, Ohio, found that the degree of stability of the pattern was greatly depen-

dent on the specific lipoprotein fractions measured. While the fraction corresponding to Gofman's S_f 12–20 fraction remained relatively unchanged, the fraction corresponding to S_f 20–100 and another fraction containing α_1 lipoproteins (not at all separable at density 1·063) revealed wide variations. Weekly measurement of the serum cholesterol level in the same normal women showed stability so long as the average level was low, but wide variations when it was above 260 mg. per 100 ml.

During a study of 107 " normal " businessmen for 7 years 11 developed cardiac infarction and another 6 angina pectoris. Comparatively small changes occurred in the serum lipid levels (at density 1·21) after infarction, but the electrophoretic pattern showed certain characteristic changes such as an increase in the concentration of fibrinogen and of the α_2 and β globulins. While the increase in α_2 globulins (only partially demonstrable by Gofman's technique) seemed to have a direct relation to the extent of myocardial damage, there was otherwise little correlation between the serum lipoprotein pattern and the severity of the infarction as measured by electrocardiographic and clinical evidence. The serum cholesterol level was higher in young men and relatively lower in the oldest age group with infarction; no similar age trends occurred in women. The range of serum lipoprotein values tended to return to normal 3 months to 10 years after infarction, though they were still somewhat higher than the mean " normal " levels. After a second infarction the changes in the electrophoretic and lipoprotein patterns were very similar to those found after the first accident.

While individual variations were unpredictable, patients with coronary atherosclerosis and a tendency to myocardial infarction—as a group—showed elevated serum cholesterol and lipoprotein levels. For this reason single estimations may be dangerously misleading, but repeated measurements of serum cholesterol and lipoprotein levels may be helpful in delineating the " coronary profile ".

[This excellent paper does not lend itself to abstracting—the more so because a substantial part of the discussion consists of an evaluation of the existing vast literature. It should be read in the original by all interested.]

Z. A. Leitner

652. **Monoamine Oxidase Inhibitors and Angina Pectoris**
T. Winsor and P. Zarco. *Angiology* [*Angiology*] **11**, 67–75, Feb., 1960. 6 figs., 22 refs.

The monoamine oxidase inhibitor iproniazid (" marsilid ") has been used widely for the relief of angina pectoris. Recent reports that serious liver damage occurs in about 1 in 4,000 patients treated with this drug, however, have stimulated trials of other inhibitors of monoamine oxidase, and this paper from the University of Southern California School of Medicine, Los Angeles, describes a trial of 4 such agents in 20 patients of an average age of 58 years who had had angina for at least one year before the trial. The four drugs were given first for 3 weeks in high dosage, which was then reduced to one-quarter to one-half of the initial level for a further 6 weeks; there were no control periods.

(1) " Nardil " (β-phenethylhydrazine hydrogen sulphate) in a dose of 45 mg. daily was given to all 20 patients, with improvement in the angina in 16 (80%). The effect was additive to that of pentaerythritol tetranitrate (80 mg. daily); there was no improvement in leg pain in 5 patients who also had intermittent claudication. (2) " Marplan " (1-benzyl-2-(5-methyl-3-*iso*xazolylcarbonyl)-hydrazine) in a dosage of 30 mg. daily also produced improvement in 80% of 15 patients, but no change in associated intermittent claudication in 4 patients. (3) Of 10 patients treated with " catron " (β-phenyl*iso*propylhydrazine), 9 were improved. (4) Six out of 8 patients receiving " niamid " (N-*iso*nicotinyl-N′-(B-N-benzyl-carboxamidoethyl)-hydrazine) had fewer attacks of angina.

The most important side-effect was postural hypotension, commonest in those who had had myocardial infarction and in those who were also receiving chlorothiazide. In no patient was there jaundice and the results of serial liver function tests, blood counts, and urine examination performed on all 20 patients were normal.

David Phear

653. **Monoamine Oxidase Inhibitors in the Treatment of Angina Pectoris**
H. I. Russek. *Angiology* [*Angiology*] **11**, 76–80, Feb., 1960. 2 figs., 17 refs.

This uncontrolled trial of 4 monoamine oxidase inhibitors for the relief of angina pectoris was carried out at the U.S. Public Health Service Hospital, Staten Island, New York, on 60 men and 26 women aged from 48 to 69 years, 27 patients receiving " marplan ", 25 " nardil ", 41 " niamid ", and 34 " tersavid ", 31 of them being treated with two or more of the drugs. The course of treatment with each drug varied from one week to 9 months.

Marplan, in a daily dosage of 30 mg., produced good relief of angina in 16 cases (59%), but side-effects were observed, postural hypotension, dizziness, constipation, restlessness, and insomnia being the most troublesome; there was no evidence in any patient of liver damage. Good relief occurred in 12 (48%) of the 25 patients given nardil, in 14 (34%) of those given niamid, and in 10 (29%) of the 34 given tersavid. Side-effects were progressively less serious as the effect of the drug on the angina decreased. There was no change in the electrocardiogram of 16 patients whose angina was improved.

It is concluded that the more active monoamine oxidase inhibitors produce more relief of angina, but also more troublesome side-effects. These drugs block pain impulses or relieve anxiety, but are thought not to improve coronary blood flow.

David Phear

654. **Preliminary Investigation of Phenelzine in the Management of Angina Pectoris**
M. Ende. *Angiology* [*Angiology*] **11**, 81–83, Feb., 1960.

The effect of phenelzine (" nardil ") in lessening angina pectoris was observed in 20 patients and its mode of action in relieving pain was investigated in 42 patients with pain due to other causes. The drug, in a dosage of 15 mg. 3 times daily, was given to the 20 patients with angina for 3 months; there was no control period. During the period of treatment 6 patients lost their pain

and 11 showed a reduction in the number of attacks of angina by at least 80%. A further patient reported 50% improvement, one had questionable improvement, but only one remained unchanged. There were no side-effects.

There was no relief of pain in 25 patients in whom it was due to a variety of other conditions, ranging from motor neurone disease to the post-gastrectomy dumping syndrome. Nor was any improvement obtained in 5 patients with tension headaches or in 12 patients with premenstrual tension and leg pain due to phlebitis.

It is suggested that the relief by phenelzine of the pain of myocardial ischaemia is not dependent on an anti-depressant effect, but is rather " of cardiac origin ".

David Phear

655. **Coronary Artery Disease: the Use of Monoamine Oxidase Inhibitors in the Treatment of the Anginal Syndrome**

C. E. Friedgood. *Angiology* [*Angiology*] **11**, 84–85, Feb., 1960. 10 refs.

At Queens Memorial Hospital, New York, " nardil " was given in a daily dosage of 45 mg. to 26 patients of an average age of 48·8 years with severe angina. The average length of known illness and previous treatment was 17 months. Many of these patients had obtained no more than transient relief from earlier treatment. In most of the cases vasodilator drugs were given concurrently.

Of the 26 patients, 21 showed marked relief of pain and only 3 were not benefited. Apart from nervousness and tachycardia in one patient there were no significant side-effects. An improvement towards a more contented mood was also noted during the treatment period. There was, however, no significant improvement in the electrocardiogram, although a moderate fall in blood pressure occurred in 4 patients. *David Phear*

656. **Effect of Nardil on Hypertension and the Anginal Syndrome**

L. F. Hobbs. *Angiology* [*Angiology*] **11**, 86–89, Feb., 1960. 11 refs.

The author reports a trial of " nardil " (phenelzine) in the treatment of 30 patients, of whom 20 had hypertension, 4 had angina pectoris, and 6 had both conditions. All were also suffering from mild or moderate depression and were selected from a group of 200 depressed patients in whom the antidepressant effects of nardil were being evaluated. In the 30 selected cases anxiety relating to the heart and blood pressure was more severe than the organic disease. The drug was given in a daily dose of 45 mg. for at least 2 months and then in a dose of 15 to 30 mg. daily according to response. There were no control periods. The previous blood-pressure levels of the 26 hypertensive patients had ranged from 150/100 to 240/125 mm. Hg. All of them had been taking hypotensive drugs for a long period before the trial, and during the trial all but 2 were also given rauwolfia drugs; the 2 exceptions were treated with diuretics alone.

After the course of nardil the blood pressure fell significantly in all but 3 patients, and in only 4 did it remain outside the normal range. Of the 10 patients with angina, 3 lost their pain and 4 reported a decrease in the number of attacks varying from 60 to 75%. There was no change in the electrocardiogram. Relief of the depression occurred in over 70% of the 30 patients, and there was an improvement in mood, with disappearance of insomnia, headaches, and tension. Side-effects were few, dizziness occurring in one patient and transient blurring of vision in another. No ill-effects resulted from the simultaneous administration of reserpine and nardil to 24 patients. *David Phear*

657. **Are the Xanthines Effective in Angina Pectoris?**

H. I. Russek. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **239**, 187–193, Feb., 1960. 1 fig., 32 refs.

The xanthine drugs have been given for the relief of angina pectoris for many years, but their value is still disputed. Aminophylline intravenously has been shown to prevent electrocardiographic changes of ischaemia after exercise, but when given by mouth it has no effect on the electrocardiogram and does not relieve angina, probably because gastro-intestinal side-effects prevent adequate dosage. A rapidly absorbed and non-irritant theophylline elixir was therefore tested at the U.S. Public Health Service Hospital, Staten Island, New York, in the treatment of 30 patients with typical angina, a double-blind technique being used. A dose of elixir containing 240 mg. of theophylline was given 3 times daily for 2 weeks to 15 patients, the remaining 15 receiving a similar inert elixir for the same period; the regimens were then reversed for a second 2-week period. This procedure was repeated over the following 4 weeks. During treatment with the theophylline elixir 76% of patient-days were recorded as associated with " no pain " or with " less pain " compared with 35·1% of patient-days with the placebo. In 16 of the 30 patients the response was " good " or " excellent " during theophylline therapy, but none showed a favourable response to the placebo. With theophylline there was a decrease in ischaemic electrocardiographic changes after exercise in 11 of the 14 patients tested.

It is concluded that the theophylline water–alcohol elixir is effective in the relief of angina pectoris.

David Phear

658. **The Treatment of Angina Pectoris with a New Prolonged Action Pentaerythritol Tetranitrate**

M. Plotz. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **239**, 194–197, Feb., 1960. 5 refs.

Pentaerythritol tetranitrate (PETN) has been widely advocated for the relief of angina pectoris. Since it usually has to be taken in a dosage of 10 to 20 mg. 3 or 4 times daily a long-acting preparation consisting of a capsule containing many tiny plastic-coated pellets of PETN which slowly dissolve in water was tried on 50 patients with typical angina. In most of the patients the dosage was 2 capsules each of 30 mg. of PETN twice a day. Of the 50 patients, 38 were able to reduce their nitroglycerine intake by at least one-third, 10 patients were unimproved, and 2 died (one from myocardial

infarction and one from cerebral thrombosis). Of 12 patients given a placebo, 2 were slightly improved. Side-effects, which subsided, included slight giddiness in 8 patients and palpitations in 2. *David Phear*

659. **Variations in Serum Lipid Concentration and Clinical Coronary Disease**

M. E. GROOVER JR., J. A. JERNIGAN, and C. D. MARTIN. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] 239, 133–139, Feb., 1960. 5 figs., 6 refs.

The results of regular clinical supervision and routine laboratory tests performed at least six times yearly for over 5 years on 177 selected individuals between the ages of 40 and 60—General Officers and civilian executives of the U.S. Air Force Headquarters—are reported. They all enjoyed excellent health at the beginning of the investigation, having been subjected to the eliminating process of regular examinations on active service. Estimations of the serum cholesterol, phospholipid, and lipoprotein levels were carried out simultaneously on aliquot parts of serum in three different laboratories. There were considerable fluctuations in the serum lipid levels, but these appeared not to be related to variations in laboratory technique.

Sixteen cases of myocardial infarction occurred in this group during the period of study. All these cases were characterized not so much by particularly high serum lipid levels, but by their excessive fluctuation. This variation amounted at times to 58 to 130% above the 5-year average for the individual patients, whereas the variation in subjects without clinical evidence of coronary heart disease amounted only to about 25%. The authors conclude, therefore, that this excessive variation in the serum lipids seems to be more significant in the prediction of the tendency to develop coronary heart disease than the actual serum lipid level.

Z. A. Leitner

BLOOD VESSELS

660. **Results of Tenotomy of the Tendo Achillis in Intermittent Claudication**

A. M. BOYD and K. BLOOR. *British Medical Journal* [*Brit. med. J.*] 1, 548–551, Feb. 20, 1960. 1 fig., 1 ref.

From the University of Manchester the authors describe the technique and after-treatment of subcutaneous tenotomy for the relief of intermittent claudication which they have employed in 72 cases. They tabulate their results under 3 headings: (1) complete relief in 16 cases (22%), including 2 cases of bilateral tendon section; (2) temporary relief for a minimum of one year in 15 cases (21%), including one of bilateral tendon section; and (3) immediate failure in 41 cases (57%), including 7 of bilateral tendon section.

The causes of failure are discussed in detail, immediate failure being ascribed to intermittent claudication occurring elsewhere in the same leg or in the opposite leg, early union of the divided tendon without lengthening, onset of ischaemic changes leading to amputation, or osteoarthritis. Discussing the principles of selection of cases for operation the authors point out that the success of the operation depends largely on the patient's intelligent, determined, and courageous cooperation, and only subjects with the right outlook should be considered. The claudication should be confined to the calf and should be of Grade 3 in their clinical grading, in which the pain on exercise increases rapidly in severity until the patient is forced to stop. In this category there is a marked tendency to spontaneous improvement in patients who have had a recent thrombosis of a main vessel and these patients should not be operated on until the absence of such improvement is certain. The nutritional state of the limb should be good enough to give no grounds for anxiety in the near future. In cases of aortico-iliac thrombosis which is causing claudication only in the calf tenotomy leads to claudication in the thigh and buttock. Patients in this category should therefore be excluded.

The authors have come to the conclusion that their high failure rate could have been greatly reduced by better selection and that the operation has a definite though limited place in the management of intermittent claudication. *Leon Gillis*

661. **The Effects of Smoking on the Peripheral Circulation**

G. M. ROTH and R. M. SHICK. *Diseases of the Chest* [*Dis. Chest*] 37, 203–210, Feb., 1960. 3 figs., 11 refs.

The effect of smoking on the peripheral circulation has been investigated at the Mayo Clinic in 100 healthy individuals and in patients with peripheral vascular disease.

In the standard smoking test finally devised and employed the skin temperature was taken as the measurement of blood flow, with simultaneous observations of the blood pressure and pulse rates. In performing the test the smokers inhaled with their accustomed depth and frequency during the 12 to 15 minutes required to smoke two-thirds of 2 commercially available cigarettes. The skin temperature of all the subjects decreased by an average of 2·5° C. (4·5° F.) at the toes and of 3·2° C. (5·8° F.) on the fingers. The mean increase in blood pressure during smoking was 20 mm. Hg systolic and 14 mm. Hg diastolic. The pulse rate increased by an average of 36 (range 20 to 52) beats per minute. Electrocardiography showed increased heart rate, decreased amplitude of the T wave, and an inverted T wave in one instance. Habitual smokers showed no signs of tolerance to the effects of smoking, the decrease in skin temperature bearing no relation to the length of time the subject had been a smoker or the number of cigarettes smoked per day. The effects of smoking on the patients with peripheral vascular disease were similar to those on normal subjects.

Experimental studies showed that nicotine was the most important factor in producing the vascular effects and that alcohol did not nullify the effect of smoking. A second group of tests was therefore carried out with various commercially available "denicotinized" cigarettes. The vascular effects, however, were similar to those produced by standard cigarettes, and this was shown to be due to the fact that the nicotine content of

such cigarettes must be decreased by more than 60% of that of standard cigarettes before smoking produces only slight or no vascular effect. The vasoconstriction of the peripheral blood vessels caused by smoking is thought to be principally mediated by the sympathetic nervous system, since in patients subjected to lumbar sympathectomy smoking produces a decrease in the skin temperature in the fingers, but not in the toes. The authors refer to tests carried out by Rehder and Roth (unpublished) in an attempt to determine whether smoking increased the production of adrenaline in men and in turn increased the blood sugar level. Smoking tests carried out on 24 normal subjects under basal conditions showed, however, that the fasting blood sugar level and that of adrenaline-like substances in the systemic blood did not rise appreciably with smoking.

A. J. Karlish

662. **The Epidemiology of Atherosclerosis.** (Epidemiologie aterosklerózy)
Z. Reiniš, D. Zoulek, J. Měšťan, K. Soukupová, J. Hrabáně, and J. Konrád. *Časopis lékařů českých* [*Čas. Lék. čes.*] **99**, 231–241, Feb. 19, 1960. 4 figs., 38 refs.

On the initiative of the World Health Organization epidemiological investigations of atherosclerosis were also started in Czechoslovakia. Using uniform international directions, a group of farmers in two Czech villages and a group population in the Far East in the regions of Chond-gin and Hai-phong were examined. Among epidemiological factors special attention was paid to dietary habits, occupation and sanitary conditions. A comparison of the biochemical properties of the blood lipids in Czech farmers and the inhabitants of the Far East revealed statistically significant differences. It can be concluded that the low blood cholesterol, phospholipid and lipid levels in Koreans and Vietnamese are related to the low energy value of the diet, its low fat content and the occupation of the population. The total cholesterol values found in the Czech farmers are, however, lower than would correspond to the caloric volume of fat according to Keys's tables. This phenomenon is probably due to their occupation where physical work plays an important part. From a comparison of the mortality rate of the inhabitants of the Czech agricultural villages and the inhabitants of the Chond-gin and Hai-phong regions it appears that atherosclerosis as a cause of death is very rare in the Far East. The mortality from atherosclerosis in Czech farmers is, however, lower than the national average mortality from this disease. As to the mortality rate from atherosclerosis of men aged 55 to 64 years, our country comes between Switzerland and Holland. This corresponds roughly to the average fat consumption of 110 g. per head per day. The authors recommended to pay attention in the comprehensive research of the aetiopathogenesis of atherosclerosis not only to dietary habits but also to other influences of the external environment, particularly to occupational factors. Comprehensive epidemiological research of atherosclerosis will require the close collaboration of most branches of medicine.—[From the authors' summary.]

663. **Acceleration of Early Stages of Coagulation in Certain Patients with Occlusive Arterial or Venous Diseases: Use of a Modified Thromboplastin Generation Test to Evaluate Clot Acceleration**
J. A. Spittel Jr., C. A. Pascuzzi, J. H. Thompson Jr., and C. A. Owen Jr. *Proceedings of the Staff Meetings of the Mayo Clinic* [*Proc. Mayo Clin.*] **35**, 37–50, Feb. 3, 1960. 1 fig., 26 refs.

The thromboplastin generation test, when suitably retarded, can be utilized to detect and roughly quantitate accelerated formation of thromboplastin. With the retarded thromboplastin generation test, accelerated formation of thromboplastin was found in 22 of 69 patients with thrombotic arterial and venous disease. The acceleration was present in the adsorbed plasma reagent but not in the serum reagent of these patients. Neither gangrene nor recent thrombus formation seemed to account for these findings. Serial studies of several patients suggested that acceleration of thromboplastin formation may be temporary (a few weeks) or permanent (at least a year). The possible causes for the acceleration are discussed.—[Authors' summary.]

664. **The Prophylaxis of Thrombosis with Fibrinolytic Agents.** (Zur Frage der Thromboseprophylaxe mit fibrinolytischen Agenten)
B. Steinmann. *Gerontologia clinica* [*Geront. clin. (Basel)*] **1**, 269–283, 1959 [received Feb., 1960]. 28 refs.

The author accepts the value of anticoagulants in the treatment of venous thrombosis and myocardial infarction, but considers that their use in cerebral thrombosis and ischaemia is still in the experimental stage. He draws attention to the many disadvantages involved and emphasizes the haemorrhagic complications. A review of recent experimental work shows that streptokinase preparations have not yet been sufficiently purified.

Nicotinic acid has been shown by several investigators to have fibrinolytic properties as well as those of vasodilatation and cholesterol regulation. After experimental investigation the drug was therefore tried in the treatment of hemiplegic patients, at first mainly by injection, but later by mouth in doses of 150 to 300 mg. daily. After a time it became evident that patients receiving this treatment had few embolic complications, the majority occurring in patients who had an underlying brain tumour or metastatic carcinoma. It was also considered that nicotinic acid administered soon after the apoplectic attack acted prophylactically. To assess the value of the drug the 241 hemiplegics treated by the author and his colleagues at the Inselspital, Berne, during the past 12 years were regarded as an experimental group, acting as their own controls. The group could not be divided into those receiving nicotinic acid and those not receiving this treatment as treatment was sporadic in many cases. The author therefore calculated the total number of patient-months in hospital represented by the group (986), divided this into 695 patient-months with and 291 patient-months without nicotinic acid therapy, and compared the incidence of complications during the two periods. Such complications occurred some 3½ times more frequently during the latter than during the former

period. Untreated patients with auricular fibrillation suffered complications 5½ times more frequently than treated patients, although auricular fibrillation predisposes to more frequent embolism. These results are considered to compare favourably with the figures reported for anticoagulant treatment, especially when the haemorrhagic complications of the latter are taken into account. There were no adverse side-effects of the use of nicotinic acid.

It is stressed that the 241 patients do not represent a homogeneous sample in which the results could be analysed statistically. During the first years of the period concerned nicotinic acid was not used and rehabilitation techniques had not been developed. The introduction of two new methods of treatment almost simultaneously makes it difficult to assess the influence of either on the basis of the figures given. On the other hand in recent years only very severe cases have been referred to the author and such cases are of their very nature more prone to embolic complications. Further work is needed to assess the minimum dosage required and to determine whether the drug dissolves an established thrombus or only prevents further clotting.

The author claims that even if his figures do not give statistical proof, it is evident that nicotinic acid is a valuable and safe method of treatment for patients suffering from cerebral thrombosis. He emphasizes the need for further research and the benefit that might ensue if nicotinic acid therapy were combined with the use of anticoagulants. *M. R. Medhurst*

HYPERTENSION

665. **Bretylium Tosylate in the Treatment of Hypertension**

C. T. Dollery, D. Emslie-Smith, and J. McMichael. *Lancet* [*Lancet*] **1**, 296–299, Feb. 6, 1960. 4 figs., 6 refs.

In this paper from the Postgraduate Medical School of London the authors report a study of 50 hypertensive patients who were given oral maintenance treatment with bretylium tosylate during a 6-month period; 28 of them had previously been treated with ganglion-blocking agents. The hypertension was of considerable severity in all patients and 22 had haemorrhages, exudates, or papilloedema on retinoscopy at the beginning of treatment; other indications for treatment were hypertension associated with chronic renal disease, hypertension in pregnancy, and hypertensive heart failure. All patients were first stabilized in hospital with bretylium in three doses totalling 600 mg. daily, increasing by 300 to 600 mg. daily until an adequate fall in blood pressure was achieved. Blood-pressure readings were taken at least four times daily with the patient both lying down and standing up. The less severely ill patients were encouraged to sit in a chair or walk about the ward as much as possible. Of 6 patients in whom the 24-hour excretion of bretylium after intravenous injection was studied, 4 who had normal renal function excreted from 65 to 83%, with a mean of 71%, but the 2 patients whose blood urea level was raised excreted only 23 and 30% respectively. However, in 10 patients who were given oral bretylium labelled with radioactive carbon the mean 24-hour excretion was only 12·9% of the administered dose. It was found that irregular and incomplete absorption after oral administration probably contributed to the variable falls of blood pressure observed in some patients, and the authors point out the danger of such unpredictable falls in patients suffering from cardiac or cerebral occlusive vascular disease.

The best results were obtained in patients whose hypertension had not progressed to papilloedema, 21 (75%) of 28 such patients being managed satisfactorily compared with only 9 (41%) of 22 patients with retinitis. Patients with malignant hypertension who had not responded to pempidine or mecamylamine almost invariably proved similarly insensitive to oral bretylium when given in the doses used in the trial (which ranged from 200 to 3,600 mg. daily). Side-effects consisting in mild nausea occurred in many patients, and 2 uraemic patients experienced vomiting which ceased on withdrawing the drug. Nasal stuffiness was frequently encountered, though only 2 patients complained of it, 4 experienced tenderness of the parotid gland at meal-times, and 3 suffered from visual impairment, probably due to accommodation difficulty: a fine papular erythematous rash developed in one patient. However, some two-thirds of the patients were not distressed to any great extent by side-effects. During the course of the trial 5 patients died, 2 of uraemia, one from dissecting aneurysm, one from cerebral haemorrhage, and one from polyneuritis. In cases in which bretylium was not being effective, even in maximum dosage, chlorothiazide or rigid sodium restriction helped to enhance its hypotensive action. However, 13 out of the 22 severe hypertensives could not be controlled by bretylium and had to be returned to treatment with ganglion-blocking agents.

In the authors' opinion bretylium tosylate is probably the first choice for "benign" hypertensive patients without ischaemic vascular disease who are being treated for the first time, but it must be regarded as less safe than pempidine or mecamylamine in patients with cerebral or myocardial ischaemia. They add that tolerance is a serious problem because the difference between the effective and the maximum dose is often small, and note also that the uncertain alimentary absorption of the drug "has a considerable bearing on the problems of treatment". *J. Warwick Buckler*

666. **Chlorothiazide and Hydrochlorothiazide in Management of Hypertension**

H. Smirk, E. G. McQueen, and R. B. I. Morrison. *British Medical Journal* [*Brit. med. J.*] **1**, 515–518, Feb. 20, 1960. 20 refs.

The authors of this paper from the Department of Medicine, University of Otago, New Zealand, report a clinical trial of chlorothiazide and hydrochlorothiazide in the treatment of hypertension. The drugs were given to 203 patients either as adjuvants to other agents or, exceptionally, as the sole form of treatment. The dosage of chlorothiazide was 500 mg. twice daily and that of hydrochlorothiazide 50 mg. twice daily. Of the 203

patients, 30 received no drugs other than chlorothiazide or hydrochlorothiazide, 26 received rauwolfia in addition, and 147 received ganglion-blocking drugs with or without rauwolfia in addition to chlorothiazide or hydrochlorothiazide. All the patients were given 1 to 2 g. of potassium chloride daily. The required dose of ganglion-blocking drugs was considerably reduced, irrespective of whether these belonged to the quaternary ammonium, the tertiary, or the secondary amine groups. Postural hypotension was often avoided by this combined regimen. In 13 patients who had previously received only rauwolfia the addition of chlorothiazide or hydrochlorothiazide brought about improved control.

Of 170 patients given chlorothiazide, 33 complained of side-effects, and of 61 given hydrochlorothiazide, 8 reported similarly; in most cases, however, these side-effects were transitory. The toxic effects were less severe with hydrochlorothiazide than with chlorothiazide except in one case of an acute sensitivity reaction. The most common complaints were nausea and epigastric discomfort. Of 19 patients who were receiving maintenance therapy with digitalis, one developed hypokalaemia with subsequent signs of digitalis poisoning.

H. F. Reichenfeld

667. **Comparison of Trimethidinium and Pempidine in Treatment of Severe Hypertension**

I. B. Houston and H. T. N. Sears. *British Medical Journal* [*Brit. med. J.*] **1**, 518–520, Feb. 20, 1960. 1 fig., 4 refs.

In this paper from the Department of Medicine, University of Manchester, a comparative study is reported of the action of two ganglion-blocking drugs, trimethidinium (a quaternary ammonium compound) and pempidine (a tertiary amine) in two groups of 12 hypertensive patients matched for age, sex, and severity of hypertension. The therapeutic dose of trimethidinium ranged from 60 to 240 mg. and that of pempidine from 5 to 60 mg. The action of the latter drug was more rapid in onset and of shorter duration than that of trimethidinium; consequently it was given 4 times daily in most cases as against twice daily for trimethidinium. Side-effects were those commonly known to be associated with ganglion-blocking drugs, the most frequent with both drugs being constipation, difficulty of accommodation, and dryness of the mouth. The constipation produced by trimethidinium appeared to be less severe than that due to pempidine; the effect of the latter drug, however, proved to be somewhat more predictable in individual patients.

From the results the authors conclude that neither drug has any definite advantage over the older ganglion-blocking agents.

H. F. Reichenfeld

668. **Chlorothiazide in Treatment of High Blood-pressure: Results of a Controlled Trial**

B. E. Juel-Jensen and M. A. Pears. *British Medical Journal* [*Brit. med. J.*] **1**, 523–527, Feb. 20, 1960. 1 fig., 1 ref.

At the Radcliffe Infirmary, Oxford, the efficacy of chlorothiazide in the control of essential hypertension was compared with that of a ganglion-blocking drug, a double-blind technique being used. A group of 15 patients were given a combination of these two drugs for 6 weeks followed by similar periods when a placebo replaced one or both. The side-effects commonly observed during administration of ganglion-blocking drugs, such as orthostatic dizziness, dryness of the mouth, blurring of vision, and constipation, were noted quite frequently when the patient was, in fact, receiving the dummy ganglion-blocking agent. A significant fall in blood pressure occurred in 5 patients when they were taking chlorothiazide alone in a dosage of 250 mg. 3 times a day. Chlorothiazide enhanced the action of mecamylamine in all 8 patients treated with the latter, but it enhanced the action of pentolinium in only one out of 7 patients.

H. F. Reichenfeld

669. **The Diagnosis and Treatment of Renal Hypertension**

E. R. Yendt, W. K. Kerr, D. R. Wilson, and Z. F. Jaworski. *American Journal of Medicine* [*Amer. J. Med.*] **22**, 169–187, Feb., 1960. 6 figs., 16 refs.

The authors discuss their experience at Toronto General Hospital during the period 1954–8 in the diagnosis and treatment of hypertension and report in detail the case of a 27-year-old woman, previously healthy, who developed hypertension (blood pressure 210/150 mm. Hg) during her third pregnancy, which terminated in abortion. An intravenous pyelogram was normal, but as the Howard test showed a reduction in urine volume and sodium concentration on the left side abdominal aortography was performed and revealed the presence of bilateral renal arterial stenosis. At operation, which took 4½ hours because of the numerous collateral vessels, the left kidney was protected by means of local hypothermia, the occluded portion of its artery resected, and the arterial stump sutured to the aorta. Postoperatively the patient remained hypertensive, although intravenous pyelography still showed good function of both kidneys. Three months later repetition of the Howard test now showed reduced urine volume and sodium concentration on the right side, and the occluded portion of the right renal artery was resected. After this operation the blood pressure fell to 135/85 mm. Hg, but 6 months later rose to 180/120 mm. Hg and there was evidence once again of right renal ischaemia. Subsequent management was with hypertensive drugs. Histological study of the resected portions of the renal arteries showed fibrous intimal thickening which split the media and extended into the adventitia, fragmentation and degeneration of the internal and external elastic laminae, and organized and recanalized thrombus occupying the lumen. In this patient inequality of the arm pulses and a bruit in the neck suggested that other arteries may have been similarly affected.

The authors have now used the differential sodium excretion test in the investigation of 125 hypertensive patients during the period mentioned. Altogether 20 cases of renal ischaemia have been diagnosed, including 6 of unilateral renal arterial stenosis, 3 of bilateral stenosis, including the case described above (and all with the same underlying pathology), 3 of renal infarction, 2

cases each of " unilateral " pyelonephritis and unilateral ureteric stenosis, and one case each of " probable renal artery lesion ", perinephric fibrosis, post-radiation nephritis, and staghorn calculus with infection. In 6 of these 20 patients the intravenous pyelogram was normal; the other 14 showed a shrunken or non-functioning kidney on one side. In 8 of the 17 cases of unilateral renal disease there was no urine flow from the affected kidney and in the other 9 the flow was reduced; of the latter 9 cases, 6 of renal artery stenosis showed reduced urinary sodium concentration, 2 of " unilateral " pyelonephritis had equal or increased sodium concentration, and one case of renal infarction showed varying sodium ratios. In the 3 cases of bilateral renal arterial stenosis there was inequality of urine volume and of sodium concentration.

In the performance of the differential sodium excretion test the authors prefer to use local anaesthesia, with collection from both ureters rather than from one ureter and the bladder and previous salt loading of the diet. Abdominal aortography was carried out as a further diagnostic aid only in selected cases. Of the 20 cases of renal ischaemia, nephrectomy was performed in 16 and vascular surgery in 4. There were 2 deaths attributable to surgery and 2 further patients died within 4 months of operation, one from myocardial infarction and one from hepatitis. The hypertension was cured or at least greatly improved by operation in 12 cases. The 4 poor results were in the female patient with bilateral renal artery stenosis described above, two cases of " unilateral " pyelonephritis, and one of renal infarction. These last 3 cases were the only ones in the series which did not show consistent reduction in sodium concentration in the urine from the diseased kidney when the Howard test was performed under proper conditions.

K. G. Lowe

670. **Effect of Thoracolumbar Sympathectomy on the Clinical Course of Primary (Essential) Hypertension**
K. A. Evelyn, M. M. Singh, W. P. Chapman, G. A. Perera, and H. Thaler. *American Journal of Medicine* [*Amer. J. Med.*] **28**, 188–221, Feb., 1960. 1 fig., 20 refs.

This paper presents an extremely careful retrospective comparison of 100 patients with essential hypertension treated by surgical sympathectomy and a matched control series symptomatically managed, all the patients having been followed up for 10 years or until death.

The surgical patients were the first 50 of each sex operated on by Smithwick's method at the Massachusetts General Hospital, Boston, between 1940 and 1945. The records of patients attending the Hypertension Clinics at the Massachusetts General Hospital, the Columbia–Presbyterian Medical Center, New York, and the Royal Victoria Hospital, Montreal, before 1945 provided a pool from which a control subject matched individually to each surgical patient was obtained. A system of numerical grading according to 5 degrees of severity (Grades 0 to 4) was devised for 14 parameters covering the blood pressure and the state of the heart, brain, kidneys, and retina in each patient, and the controls were selected to match the sex, age, and grading of the surgical patients in their preoperative state. The grading of each patient, derived from the case records, was then recorded for the initial state and 2 years, 5 years, and 10 years later. For each parameter progress was recorded by writing down the four digits representing the grade in that parameter at each of the four chosen stages over the 10-year period. A vast amount of information is thus compressed into a table describing all the 100 pairs of cases and this information is discussed at length. Comparison of the initial states of the surgical and control patients shows a truly remarkable degree of matching. The difficulties encountered in making the numerical gradings from the case records are fully discussed. [This mass of information and comment cannot be compressed within the space of an abstract and should be read in the original by all who are interested in the treatment of hypertension.]

The data presented give the impression that relatively little was achieved by surgical sympathectomy, though a slight advantage has accrued to these patients. This is the conclusion of the authors, who comment that " on the whole therefore it would appear that the general clinical condition of the average surgically treated patient who was still alive at the end of ten years was only slightly better than that of the average survivor in the control series ". Among the surgical cases, however, there were some who were greatly improved, whereas such unequivocal improvement was not observed in any case in the control series.

[The investigation here reported is an important contribution to the assessment of the results of treatment for essential hypertension. The authors intend to prepare numerically graded records of a substantial number of their control subjects for use in future studies of drug therapy.] *C. J. Longland*

671. **Unilateral Chronic Pyelonephritis and Hypertension.** (Односторонний хронический пиелонефрит и гипертония)
A. Ja. Pytel'. *Урология* [*Urologija*] **5**, 3–17, Jan.–Feb., 1960. 5 figs.

The author analyses the literature on hypertension due to unilateral chronic pyelonephritis and records his experience of 126 patients with chronic pyelonephritis, of whom 31 had unilateral disease. Of these 31 cases, 8 were complicated by severe hypertension, and nephrectomy was performed in 5 (all in women). The blood pressure returned to normal in 4, while in the remaining one only temporary improvement was noted.

He describes the clinical features and investigation of these cases, stressing the difficulty of reaching a diagnosis early enough to affect the course of hypertension by nephrectomy. He urges the importance of renal angiography and describes the characteristic appearance of the affected kidney. The density of the renal shadow is less than normal and patchy. The renal vessels are narrowed and in particular the segmental vessels show a deficiency of parenchymal branches, giving a " burned tree " appearance. Demonstration of these radiographic signs may allow operation to be performed early enough to effect a cure. *N. Hopewell*

Clinical Haematology

672. **A Peanut Factor for Haemostasis in Haemophilia**
H. B. BOUDREAUX and V. L. FRAMPTON. *Nature* [*Nature (Lond.)*] **185**, 469–470, Feb. 13, 1960. 9 refs.

In this paper from the Louisiana State University, Baton Rouge, and the U.S. Department of Agriculture, New Orleans, it is postulated that if the basis of haemophilia is defective synthesis of some precursor essential to elaboration of antihaemophilic globulin it might be possible to supply the essential substance by mouth or by injection. The senior author of this preliminary communication suffers from haemophilia. In the course of personal observations on the influence of various foods on the activity of the disease, he noted improvement apparently related to ingestion of peanuts. Over a 2-year period the bleeding tendency recurred whenever peanut products were avoided, the recurrence yielding within 48 to 72 hours of resuming the peanut regimen. The improvement was not associated with reduction of capillary or venous blood clotting time. No other study *in vitro* was made. The active principle was extractable with 90% ethyl alcohol and the effective dose was equivalent to about 1 lb. (0·45 kg.) of peanuts a day. Consistent results are claimed to have been obtained in 3 volunteers. *A. Brown*

673. **The Role of the Kidney in Erythropoiesis**
J. P. NAETS. *Journal of Clinical Investigation* [*J. clin. Invest.*] **39**, 102–110, Jan., 1960. 3 figs., 39 refs.

Various investigators have attributed the mechanism of uraemic anaemia to the double effects of shortened erythrocyte survival and depression of erythropoiesis, but more recent work has suggested that the kidney itself may be the source of an erythropoietic factor. At the Hôpital Brugmann, Brussels, the author has investigated the latter possibility experimentally in dogs, 15 of which were subjected to bilateral nephrectomy (carried out in 2 stages) and 9 to bilateral ligation of the ureters or unilateral nephrectomy with ureteric ligation on the opposite side. Of the 12 control animals, 9 were left normal and intact and 3 were subjected to unilateral nephrectomy. The uraemic dogs were maintained for 7 to 15 days by peritoneal lavage which was begun 72 hours after the second nephrectomy or ureteric ligation.

Despite the fact that the plasma urea and potassium levels showed similar elevation in both the bilaterally nephrectomized and the ureter-ligated dogs and the resulting anorexia produced a similar state of starvation in both groups, the haematological pictures differed. Thus bilateral ureteric ligation was not attended by any severe haematological disturbance. Although the normoblast count in the marrow tended to decrease, the reticulocyte count was often within normal values. There was a reduction in the turnover of iron in the plasma, but this was less marked than in the nephrectomized dogs, while the uptake of radioactive iron (^{59}Fe) was of the same order as in the control group. In contrast, bilateral nephrectomy produced a rapid depletion of the marrow normoblasts, with complete disappearance of these cells after 72 hours, and 5 days after nephrectomy no reticulocytes were seen in the peripheral blood. In 2 dogs which were severely bled no marrow response occurred. The plasma turnover of iron was significantly reduced in this group and incorporation of ^{59}Fe was practically abolished, whereas there was increased storage of iron in the liver. In one of the bilaterally nephrectomized dogs which was given a marrow erythropoietic factor intravenously a normal erythroblastic marrow picture was maintained.

The author concludes that the haematological changes induced by total nephrectomy cannot be accounted for solely by the retention of toxins and considers it likely that the kidney is the source of an erythropoietic factor.
D. G. Adamson

ANAEMIA

674. **Iron Therapy in Chronically Fatigued, Nonanemic Women: a Double-blind Study**
E. BEUTLER, S. E. LARSH, and C. W. GURNEY. *Annals of Internal Medicine* [*Ann. intern. Med.*] **52**, 378–394, Feb., 1960. 5 figs., 36 refs.

A brief review of the literature has shown that various workers in the past century have suggested that some women who complain of chronic fatigue may be suffering from iron deficiency although they are not anaemic. At the University of Chicago the present authors have carried out a carefully controlled trial of the effect of iron on 30 chronically tired women whose haemoglobin value exceeded 12 g. per 100 ml. To half the subjects, selected by chance, tablets of ferrous sulphate were first given for 3 months, then no therapy during the next month, followed by the placebo tablets (bismuth subcarbonate) for a further 3 months; for the other half this order was reversed. Each patient was examined monthly, just after her menstrual period, the data recorded including the patient's symptoms and haemoglobin level at the various stages of the trial, at the beginning of which the iron store in the bone marrow was assessed.

In those patients with subnormal iron stores in the marrow, even although the haemoglobin value was within the normal range, the iron store was increased by ferrous sulphate therapy, but not by the placebo. Almost all the subjects admitted to some improvement in symptoms, but it was only those with depleted stores of iron in the marrow who showed a significantly greater response to iron than to the placebo; thus of 18 iron-depleted patients, 13 showed more improvement during iron therapy and 5 during placebo medication. The authors suggest that their results lend weight to the hypo-

thesis that a syndrome of fatigue in women may be due to a degree of iron deficiency without anaemia, but further study on a larger number of patients is required to confirm this. *T. B. Begg*

675. **Pernicious Anemia in Childhood**
S. L. LEIKIN. *Pediatrics* [*Pediatrics*] **25**, 91–100, Jan., 1960. 3 figs., 18 refs.

The cases are reported of two coloured sibs, a girl of 2½ years and a boy of 2 years, both of whom had macrocytic anaemia with the morphological changes of pernicious anaemia, megaloblastosis of the marrow, and a very low serum vitamin-B_{12} (cyanocobalamin) level. They responded to parenteral vitamin-B_{12} therapy with an adequate reticulocytosis, a reversion to normoblastic erythropoiesis, and a satisfactory rise in the erythrocyte count and haemoglobin value, the serum vitamin-B_{12} level becoming normal. In both cases there was defective absorption of radioactive vitamin-B_{12} (Schilling test) which became normal on administration of intrinsic factor. Gastric juice from one patient failed to show intrinsic-factor activity when given with radioactive vitamin B_{12} to a patient with proven pernicious anaemia.

Before treatment neither patient showed "free" hydrochloric acid in the fasting gastric juice, but both responded to histamine (fasting *p*H 6·4 in both cases, changing to 1·0 and 2·4 respectively after histamine). After treatment both had "free" acid in the gastric juice. The gastric mucosa of both patients was normal on biopsy; neither had glossitis. No evidence of malabsorption syndrome was found on very adequate investigation. In one case a jejunal biopsy was performed, with normal findings. The author concludes that "the gastric manifestations of pernicious anaemia are not an intrinsic part of the disease" and suggests that the atrophy may be secondary to long-standing vitamin-B_{12} deficiency. *R. B. Thompson*

676. **Studies on the Haemoglobin of Newborn Nigerians**
R. G. HENDRICKSE, A. E. BOYO, P. A. FITZGERALD, and S. R. KUTI. *British Medical Journal* [*Brit. med. J.*] **1**, 611–614, Feb. 27, 1960. 6 figs., 16 refs.

The cord blood of 100 newborn Nigerians was investigated at University College Hospital, Ibadan, Nigeria, for abnormal haemoglobins. Sickling was found in 5 at birth and in a further 6 by the second month. Of these 11 children, 7 showed sickle-cell trait and one sickle-cell–haemoglobin-C disease. The proportion of foetal haemoglobin ranged from 45 to 96% at birth and fell to 10 to 20% by the third month in the whole group, the range being similar in those showing sickling. The presence of foetal haemoglobin obscured the true adult haemoglobin pattern on electrophoresis at *p*H 8·6 of the specimens taken at birth and during the first few months, except for haemoglobin C. However, in 11 out of the 100 specimens of cord blood studied a fast-moving haemoglobin was detected which persisted for 2 months. There was no correlation between the presence of this fast haemoglobin and the child's sex, birth weight, or genotype or the mother's genotype or tribe. Further investigation in 3 cases showed the fast haemoglobin to resemble haemoglobin "Bart's" in one case and the haemoglobin of Fessas and Papaspyrou in the others. *M. Lubran*

677. **Refractory Anemia with Hyperplastic Bone Marrow**
R. W. VILTER, T. JARROLD, J. J. WILL, J. F. MUELLER, B. I. FRIEDMAN, and V.. R. HAWKINS. *Blood* [*Blood*] **15**, 1–29, Jan., 1960. 6 figs., 49 refs.

Cases of refractory anaemia with hyperplastic bone marrow are rare. Over a recent 16-year period the authors have had an opportunity of studying 23 cases of this type and their observations are reported in this paper from the College of Medicine, the General Hospital, and the Veterans Administration Hospital, Cincinnati, Ohio. During the study it became clear that these cases could be tentatively classified into five types. It is admitted that these groupings are probably highly artificial, but they are made to facilitate presentation and description. The marrow may show normoblastic hyperplasia, hypoplasia, or even aplasia. In other cases pancytopenia is present, with or without a bizarre chromatin pattern in the normoblast. In 2 cases there was a frankly megaloblastic bone marrow with free hydrochloric acid in the gastric secretion.

After reviewing the literature the authors put forward hypotheses to explain these various types of anaemia on the basis of abnormalities in the metabolism of nucleic acids, particularly deoxyribonucleic acid. *A. W. H. Foxell*

NEOPLASTIC DISEASES

678. **Hodgkin's Disease With and Without Alcohol-induced Pain: a Clinical and Histological Comparison**
A. H. JAMES. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **29**, 47–66, Jan. [received May], 1960. 3 figs., 29 refs.

In 1950 Hoster (*Amer. J. Roentgenol.*, **64**, 613) first drew attention to the observation that some patients with Hodgkin's disease experience pain at one or more sites of the disease after taking an alcoholic drink, and the present author lists 58 cases reported in the literature since that time. The pain usually starts some minutes after the drink, lasts for a variable period (up to some hours), and may vary considerably in intensity. Successful treatment of the disease abolishes the occurrence of this alcohol-induced pain. A study of nine reported series, totalling 205 cases, showed that the symptom occurred in 35, an incidence of about 17%. In the present paper from the Royal Infirmary, Cardiff, the author reports a study of the clinical histories and histological findings in 33 patients with Hodgkin's disease, of whom 13 suffered from pain after taking alcohol. Histological sections of lymph-node biopsy specimens taken from various sites were examined by three pathologists independently who were unaware of the patients' clinical history and who used an agreed scoring system for recording features.

The conclusions reached were that in the early stages of Hodgkin's disease patients who suffer from alcohol-

induced pain more often also have spontaneous pain in one or more diseased areas, show a leucocytosis, and exhibit mediastinal involvement. Sections from the affected lymph nodes of these patients tended to show fewer reticulum-cell mitoses, more eosinophil granulocytes, and more fibrosis. The author points out that the proportion of men among the patients with alcohol-induced pain (52·5%) was lower than that among all patients with Hodgkin's disease (69·8%) and discusses his reasons for suggesting that patients who suffer pain after alcohol have either a separate disease or a distinct form of Hodgkin's disease with the features described above. He considers that it is likely that alcohol-induced pain does not occur exclusively in Hodgkin's disease, for the symptom has been reported in other malignant conditions and also in lesions involving bone.

M. C. G. Israëls

679. **Serum Hexosamine Level in the Diagnosis of Hodgkin's Disease**

S. WEIDEN. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 207–209, Feb. 6, 1960. 3 figs., 9 refs.

The diagnostic value of an increased serum hexosamine level in Hodgkin's disease was studied at the Walter and Eliza Hall Institute of Medical Research and the Royal Melbourne Hospital, Melbourne. In 46 normal subjects the level ranged from 80 to 124 mg. per 100 ml. (mean 101·5±11 mg. per 100 ml.). It was over 200 mg. per 100 ml. in 5 out of 6 patients with untreated Hodgkin's disease and was 148 mg. per 100 ml. in the sixth. The values fell below 160 mg. per 100 ml. in 8 treated patients with Hodgkin's disease. Normal values were found in leukaemia (11 patients) and disseminated lupus erythematosus (9 patients), and normal or slightly raised values (all less than 160 mg. per 100 ml.) in 46 patients with various active infections and 32 patients with diabetes mellitus. Raised values were found in all of 3 patients with macroglobulinaemia, in 7 out of 15 patients with carcinoma of various types, and 6 out of 16 patients with rheumatoid arthritis.

It is concluded that the finding of a very high serum hexosamine level may be of value in distinguishing Hodgkin's disease from chronic infections and other conditions, such as leukaemia, which may present a difficult diagnostic problem. *M. Lubran*

680. **Hodgkin's Disease: a Maternal-to-foetal Lymphocyte Chimaera? (Preliminary Communication)**

I. GREEN, M. INKELAS, and L. B. ALLEN. *Lancet* [*Lancet*] **1**, 30–32, Jan. 2, 1960. 28 refs.

From the Montefiore Hospital, New York, the authors put forward a hypothesis of the causation of Hodgkin's disease based on the phenomenon of acquired tolerance, the probable ability of maternal lymphocytes to reach the foetal circulation, and the immunological theory of carcinogenesis.

Acquired tolerance occurs when an animal is exposed to antigenic stimuli before the immunological response has developed. Thus if maternal leucocytes could enter the foetal circulation when the foetus is immunologically tolerant these cells could survive and reproduce and the mature foetus would then be a lymphocyte chimaera. Experimentally, radiation chimaeras and chimaeras produced by injecting newborn, tolerant mice with homologous lymphocytes produces homologous ("runt") disease which has certain characteristics similar to those of Hodgkin's disease. It is suggested that a transfer of maternal lymphocytes to the foetus is feasible in view of the long survival time of these cells and since erythrocytes, which match small lymphocytes in size, and cancer cells, which are larger, can pass the placental barrier. In the imperfect, partially tolerant lymphocyte chimaera there may occur an alteration in the antigenic properties of the identity proteins of the transferred maternal lymphocytes so that autoimmunization occurs with subsequent malignant change. Since all the transplantation antigens of the skin are also present in the lymphocytes, the chimaeral patient should show some degree of tolerance to maternal skin. This postulate was tested in 5 male patients suffering from Hodgkin's disease who were homografted with maternal skin. Prolonged survival of the maternal homograft was observed in 2 of the 5.

The authors appreciate that several possible explanations, apart from acquired tolerance, could account for the prolonged survival of maternal grafts in patients with Hodgkin's disease, but suggest that further investigations should be made to test the validity of the above hypothesis. *D. G. Adamson*

681. **Urticaria Pigmentosa with Visceral and Skeletal Lesions**

C. W. H. HAVARD and R. BODLEY SCOTT. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **28**, 459–470, Oct., 1959 [received March, 1960]. 8 figs., bibliography.

In urticaria pigmentosa a typical skin eruption is associated with proliferation of mast cells in the skin. When visceral lesions occur, as in some cases, there may be enlargement of lymph nodes, liver, and spleen, skeletal changes, and abnormalities of coagulation. The pathological basis for these lesions is proliferation of mast cells in the viscera, with a secondary fibrous tissue reaction and consequent cirrhosis of the liver or myelofibrosis. The haemorrhagic manifestations can usually be ascribed to liver damage or thrombocytopenia. The course of the disease is relatively benign.

The authors describe a case, that of a man aged 67 admitted to St. Bartholomew's Hospital, London, with a typical skin rash, splenic and hepatic enlargement, and bone changes which were radiologically and histologically typical. The skin eruption had first appeared 12 years previously. Oesophageal varices were demonstrated radiologically. Other findings were anaemia with thrombocytopenia, a raised serum calcium level, and a lowered serum inorganic phosphate level. During the next 2 years the results of liver function tests showed progressive impairment, and fat-balance tests revealed only 55% absorption. Bone pain was severe and was relieved by irradiation. The authors review 19 cases of urticaria pigmentosa with visceral involvement reported in the literature and discuss the pathological and clinical features of this condition, which they regard as a "mast-cell reticulosis". *J. L. Markson*

Respiratory System

682. **Haemoptysis**
R. N. JOHNSTON, W. LOCKHART, R. T. RITCHIE, and D. H. SMITH. *British Medical Journal* [*Brit. med. J.*] **1**, 592–595, Feb. 27, 1960. 3 refs.

Of 2,187 new patients attending the Chest Clinic, Dundee, during 1956, 324 (15%) gave a history of haemoptysis in the preceding month. The majority were young, the peak incidence occurring in the 3rd decade. The final diagnoses included upper respiratory-tract infection, bronchitis, or pneumonia in 153 patients, bronchiectasis in 43, and carcinoma and active tuberculosis each in 14 patients only. There was no abnormality in 68 patients.

Only minor differences were observed in the character of the haemoptysis in the various diseases. In patients with active tuberculosis or bronchiectasis the haemoptysis was brisk and of short duration, whereas in patients with carcinoma it was more prolonged, and in about a quarter of them it was classified as " not certain ". In chronic bronchitis there was no distinctive pattern; usually the haemoptysis was " certain "—a single episode with only streaking of the sputum.

Over the 2-year follow-up period 20 patients died. Of the remaining 304, 279 were re-examined at one year and 273 at the end of 2 years. Of the 31 not examined at 2 years, 10 refused further x-ray examination. It is of interest that at the follow-up examination several of the patients denied the previous haemoptysis. The diagnosis had to be corrected in 3 cases: in one the original diagnosis was bronchitis, but later a carcinoma of the bronchus was found; in another, which was kept under observation because of " minimal observation pulmonary tubercle ", cavitation developed; and in the third the chest radiograph was normal originally, but 10 months later there was a minimal focus in the right upper zone with positive sputum. A further patient with a suspicious left hilar shadow refused investigation, but 11 months later an inoperable carcinoma of the bronchus was found. Despite these 4 cases the authors conclude that follow-up examination in cases of haemoptysis is not necessary provided patients are carefully assessed originally. In men over the age of 40, in whom the risk of carcinoma is higher, bronchoscopy is an essential part of the initial investigation. *A. Gordon Beckett*

683. **Open Lung Biopsy for Diffuse Pulmonary Lesions**
L. J. GRANT and S. A. TRIVEDI. *British Medical Journal* [*Brit. med. J.*] **1**, 17–21, Jan. 2, 1960. 28 refs.

The authors describe in detail the method used for lung biopsy at the London Chest Hospital. A small antero-lateral incision is made and the opportunity is taken to examine the whole lung and the mediastinal lymph nodes. A node and a portion of that part of the lung showing most disease are removed. The details of 26 cases in which this procedure was used are given in tabular form. In only 2 was the histological report indefinite, and in several cases unexpected diagnoses became apparent.

The authors discuss the various methods which have been described for obtaining pieces of lung for histological examination and state their conviction that open operation is the method of choice. In the series reported there was no mortality and the morbidity was slight, whereas with other methods, such as needle biopsy, there is a definite mortality and the results are often unsatisfactory. They also consider that their method is more likely to give positive results than scalene-node biopsy unless the lymph nodes are palpable. They finish by reporting a number of illustrative cases in which the procedure was shown to be of clinical as well as of academic value. *J. R. Belcher*

684. **Chronic Diffuse Interstitial Fibrosis of the Lungs**
J. G. SCADDING. *British Medical Journal* [*Brit. med. J.*] **1**, 443–450, Feb. 13, 1960. 7 figs., 15 refs.

From the Institute of Diseases of the Chest, Brompton Hospital, London, the author describes a condition which he terms " idiopathic chronic diffuse interstitial fibrosis of the lungs ", of which he has seen 26 cases between 1950 and 1959. If cases of diffuse pulmonary fibrosis of known aetiology, such as those due to sarcoidosis, tuberculosis, or dust diseases, are eliminated a group is left of which the larger proportion presents a typical syndrome with distinct clinical, radiological, and physiological features which cannot be explained as resulting from an otherwise recognized pathological process. He distinguishes this condition from the acute interstitial fibrosis of the lungs described by Hamman and Rich; the latter is more acute, affects patients of a younger age group, and shows different lesions histologically. Whether the two types are related is unknown. The chronic fibrosis is more common than the acute.

In the author's series males and females were equally affected, only 3 patients were under 50, and the average age was 53½ years. The picture presented is that of a middle-aged or elderly patient, previously well, who complains of progressive breathlessness for several years; there is a cough which may be unproductive but is often troublesome, cyanosis at first after exertion and later at rest, and almost invariably gross clubbing of the fingers, which may be a presenting symptom. Examination reveals no cardiac lesion and no constitutional upset, but there is hyperventilation, an impaired percussion note, and persistent rales at the lung bases, while radiography reveals a nodular or reticular pattern (and later " honeycombing ") throughout both lungs which is not symmetrical. Tests show that the defect is one of diffusion between the alveolar air and the alveolar capillaries, there being no obstruction of the airways. Histologically, there is chronic inflammation and fibrosis of the alveolar walls, with proliferation of the lining cells which in one case was indistinguishable from alveolar-

cell carcinoma. Bronchography shows the bronchi to be patent much further towards the periphery than usual and the unfilled peripheral zone is narrowed. Discussing the aetiology of the condition the author comments on the striking similarities and differences between the lung changes in this syndrome and those due to chemical irritants or in virus diseases and the collagen diseases and suggests that auto-immunity must be considered as a possible cause, pointing out in support of this view that one of his patients had hepatomegaly with granulomatous infiltration of the portal tracts and the sister of another showed similar changes in the liver.

The author has treated 12 of these patients with corticosteroids, with good results in one, some improvement in 4, and no improvement in 4, one of whom later died. He points out that steroid therapy, once started, may have to be continued indefinitely, since withdrawal may produce severe or fatal symptoms. Intercurrent infection must be treated as it arises, otherwise the course of the disease is steadily downhill with occasional "remissions", that is, periods in which the disorder does not progress. The acuteness and rate of progress roughly vary inversely with the age of the patient.

Janet Q. Ballantine

685. **Simplification of Haldane's Apparatus for Measuring CO_2 Concentration in Respired Gases in Clinical Practice**

E. J. M. CAMPBELL. *British Medical Journal* [*Brit. med. J.*] **1**, 457–458, Feb. 13, 1960. 1 fig., 3 refs.

By the removal of the oxygen absorption pipette and substitution of a three-way tap for the two-way tap and of a syringe for the mercury levelling bulb in the Haldane respiratory gas analysis apparatus a simple and convenient apparatus for measuring the carbon dioxide concentration in respired gases is provided. The method of use of the apparatus is described step by step and the author claims for it portability, speed, ease of servicing, cheapness, and a reasonable degree of accuracy.

J. Robertson Sinton

686. **Simple Rapid Methods of Estimating Arterial and Mixed Venous pCO_2**

E. J. M. CAMPBELL and J. B. L. HOWELL. *British Medical Journal* [*Brit. med. J.*] **1**, 458–462, Feb. 13, 1960. 3 figs., 12 refs.

The complicated nature of available methods of estimating the pressure of carbon dioxide (pCO_2) contained in arterial and mixed venous blood has hitherto prevented the wider use in clinical medicine of knowledge of this important physiological value. The authors of this paper from the Middlesex Hospital, London, describe an indirect method of estimating the pCO_2 by analysis of the CO_2 content of small quantities of gases that have been rebreathed for 20 or 40 seconds and claim agreement within 3 mm. Hg with the results of direct pCO_2 measurements by Riley's method and those provided by Haldane's indirect method of analysis of alveolar air. They report the results of estimations performed in 15 cases of respiratory and metabolic disease by their modification of Collier's rebreathing method controlled by a continuous CO_2 analyser and by direct estimations from arterial blood. The method involves the inhalation of gas from a small series of bags containing known proportions of CO_2. The CO_2 content of mixed venous blood is obtained by analysis of the bag which initially contained a slightly higher CO_2 content than that in the alveoli, and the arterial pCO_2 is taken to be 6 mm. Hg higher than that of mixed venous blood.

J. Robertson Sinton

687. **Changes in Forced Expiratory Volumes throughout the Day**

H. C. LEWINSOHN, L. H. CAPEL, and J. SMART. *British Medical Journal* [*Brit. med. J.*] **1**, 462–464, Feb. 13, 1960. 3 figs., 2 refs.

Estimations of the forced expiratory volume (F.E.V.) and of the forced vital capacity (F.V.C.) were made at the London Chest Hospital at different times during the course of the day on 5 normal males and 16 male patients with moderate or severe obstructive airway disease. These functions were shown to be lowest on waking, to have increased substantially by 9 a.m., and to diminish post-prandially in the early afternoon, recovering in the evening. The early morning decrease in F.E.V. and F.V.C. was greater in the patients than in normal subjects, a finding which accords with the common complaint of patients with chronic bronchitis that they are at their worst in the early morning. It is pointed out that the relatively large spontaneous variations in the F.E.V. and F.V.C. of patients with obstructive airway disease "might affect the interpretation of results when serial changes in these volumes are used to measure the action of drugs on the bronchial tree". *J. Robertson Sinton*

688. **Pulmonary Ventilatory Function in Military Recruits during Health and Acute Viral Respiratory Disease, Including Pneumonia**

R. B. STONEHILL, N. SCHALET, W. Y. FONG, H. SALTZMAN, and H. B. HOUSER. *American Review of Respiratory Diseases* [*Amer. Rev. resp. Dis.*] **81**, 315–320, March, 1960. 7 refs.

The pulmonary ventilatory function tests of maximal breathing capacity, vital capacity, and one-second and three-second vital capacities were performed serially at 2- to 3-week intervals for 11 weeks in a group of 60 Air Force recruits. Moderately severe acute respiratory disease occurred in 34 men, 14 of whom also had evidence of pulmonary infiltration of mild degree by roentgenographic examination. The remaining 26 men remained free of respiratory infection by the criteria established.

The only test that showed significant change at any of the periods of observation was the vital capacity. Although a significant decrease in vital capacity occurred on one occasion in the group without respiratory disease, those patients with pulmonary infiltration showed a more marked decrease during the time of their illness.

The reproducibility of the tests, even in the presence of respiratory disease without pneumonia, indicates that considerable confidence can be had that significant variation in the results will not occur in multiple tests in an individual because of technical reasons.—[Authors' summary.]

Urogenital System

689. **Renal Tubular Disease with Muscle Paralysis and Hypokalemia**

E. E. Owen and J. V. Verner Jr. *American Journal of Medicine* [*Amer. J. Med.*] **28**, 8–21, Jan., 1960. Bibliography.

This paper from Duke University Medical Center, Durham, N. Carolina, reports and comments on the cases of 10 patients who showed the combination of renal tubular disease, low serum potassium concentration, and episodic muscle paralysis. There is a general discussion and a review of the literature on potassium-losing renal disease. Eight of the 10 patients had pyelonephritis, but whether this was a cause or a complication could not be established. Treatment of the metabolic losses with potassium and alkali and of recurrent urinary infection with antibiotics controlled the symptoms and seemed to arrest the progress of renal damage.

D. A. K. Black

690. **Clinical Course of Uncomplicated Acute Tubular Necrosis**

L. W. Loughridge, M. D. Milne, R. Shackman, and I. D. P. Wootton. *Lancet* [*Lancet*] **1**, 351–355, Feb. 13, 1960. 6 figs., 10 refs.

The mortality from acute tubular necrosis is high when the condition is associated with severe injuries to the tissues or the trauma of surgical operation. In order to analyse the course of acute tubular necrosis uncomplicated by these added factors the authors have studied, at Hammersmith Hospital (Postgraduate Medical School of London), a selected group of 28 such cases in which there was complete recovery. During the period of this study 11 other patients diagnosed on admission as having uncomplicated acute tubular necrosis died; in 3 there was almost complete renal cortical necrosis, while the most common cause of death in the remainder was sepsis.

All the 28 patients studied were treated by a standard regimen consisting in the administration of a 20% lactose solution by mouth in a volume of X+400 ml. daily in the winter months and X+500 ml. daily in the summer months (May to October), X being the total volume of measurable fluid lost from the body on the previous day. If intractable uraemic vomiting occurred the same volume of a sterile 40% glucose solution was given by intravenous infusion, usually into the superior vena cava. Soluble insulin was given if the blood sugar level exceeded 200 mg. per 100 ml. The patients were isolated and "barrier nursed" and those with proved infection were treated with antibiotics or sulphonamides. The haemoglobin value was maintained above 10·2 g. per litre (70% Haldane) by infusions of packed cells. Haemodialysis with a rotating-drum artificial kidney was carried out (in 13 cases) if: (1) the blood urea level rose above 400 mg. per 100 ml.; (2) the plasma potassium level rose above 7·5 mEq. per litre; (3) the alkali reserve fell below 12 mEq. per 1 litre; (4) the electrocardiogram showed evidence of intraventricular block; or (5) vomiting, hiccup, uraemic stupor, or fits developed.

The course of recovery could be divided into three phases—the oliguric, the early diuretic, and the late diuretic. The mean duration of the oliguric phase, that is, the period during which less than 400 ml. of urine was passed daily, was 12·5 days; complete anuria was extremely rare. During the first 6 days of this period the calculated mean daily urinary volume was only 75 ml., with a mean of 150 ml. for the whole period. The mean blood urea level rose to 200 mg. per 100 ml. by the end of the second day, reflecting increased catabolism, but thereafter the rate of rise averaged 34 mg. per 100 ml. per day. The oliguric phase was followed by an early diuretic phase with a mean duration of 4·7 days during which the daily volume of urine increased from 400 to 2,000 ml., but the blood urea level did not fall. In the late diuretic phase the volume of urine excreted remained stable at 2,000 to 2,500 ml. daily and the blood urea level fell to normal over 17 days.

At the end of the late diuretic phase, after an illness of about 5 weeks during which there has been little or no intake of protein, the patient has lost at least 1·5 kg. of body protein (about one-eighth of the total body content); a period of 2 or 3 months' convalescence is needed before he can return to full activity. In uncomplicated cases the course of the oliguric stage can usually be accurately predicted after a few days' careful observation, but in cases with severe tissue damage the course is unpredictable. The paper concludes with some brief notes on the 11 fatal cases mentioned above.

David Phear

691. **A Study of Distal Renal Tubular Functions by a Modified Stop Flow Technique**

J. R. Jaenike and R. W. Berliner. *Journal of Clinical Investigation* [*J. clin. Invest.*] **39**, 481–490, March, 1960. 5 figs., 22 refs.

Using a modified stop flow technique, the authors studied distal renal tubular function in dogs under various experimental conditions at the National Heart Institute, Bethesda, Maryland. The presence of 2 to 3 ml. of urine in the dead space within the renal pelvis distorts the concentration patterns in specimens from the distal tubular segments. This was overcome by filling and emptying the renal pelvis with air through a ureteral catheter to wash out the urine and then running in mineral oil until a pressure of 100 mm. Hg was attained. This pressure was maintained throughout the stop flow period to prevent the entrance of newly formed urine into the pelvis from the kidney. In order to localize the specimen in relation to the distal convoluted tubule an attempt was made to label the urine contained within the renal cortex during the occlusion period. A needle was introduced into the superficial renal cortex and radioactive potassium in the form of ^{42}KCl was injected. The stop flow specimens were then counted in a well-type scintillation coun-

ter. The absence of isotope in the first specimens collected indicated that these came from the medullary or inner cortical portion of the distal tubules. ^{42}K then appeared in a sharp peak and later diminished, presumably because of more rapid urinary transit through the area containing the isotope and because of removal of isotope in the renal circulation.

The authors summarize their findings as follows. "In accord with previous studies, the data suggest that the epithelium of the distal convolution is highly permeable to water in the presence of vasopressin. In contrast, during water diuresis, a considerable restriction to the diffusion of water is exhibited in the same area. It has been shown that water diffuses out of the collecting ducts in the absence of vasopressin, as has been concluded by previous workers. Sodium chloride reabsorption occurs in the region of the distal convoluted tubule. Under certain conditions this process may occur against a high electrochemical gradient. It has been demonstrated that vasopressin-dependent water permeability and sodium chloride reabsorption occur coextensively, apparently in the cortical area of the distal tubular system. This association results in an effective reduction in the volume of fluid delivered to the concentrating area, and consequently enhances the ability of the kidney to elaborate a highly concentrated urine. Potassium secretion occurs in the distal tubular system during ureteral occlusion. It is suggested that previous conclusions as to the presence of a potassium reabsorptive mechanism in the distal tubule are erroneous, since the data were obtained under conditions in which the sodium concentration of the tubular fluid was extremely low, thereby imposing a limit on subsequent cation exchange, potassium for sodium." *G. W. Csonka*

692. **Glomerulonephritis in Older Age Groups**
H. R. Nesson and S. L. Robbins. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **105**, 23–32, Jan., 1960. 3 figs., 28 refs.

The records of 11,157 cases in which necropsy was performed over a 12-year period at the Mallory Institute of Pathology, Boston City Hospital, were examined to determine the incidence of glomerulonephritis, the importance of this disease as a cause of death at various ages, and whether the clinical manifestations of glomerulonephritis arising in later life differ from those in children. Glomerulonephritis was diagnosed post mortem in 108 (0·97%) cases and pyelonephritis in 1,073 (9·6%). Death was due primarily to renal disease in 76·8% of the cases of glomerulonephritis and 29·8% of those of pyelonephritis. Over 70% of the fatal cases of glomerulonephritis occurred in patients over the age of 40 (87% of the patients with acute glomerulonephritis were in this age group). Of the 74 cases of glomerulonephritis studied in some detail, the condition was diagnosed anatomically as acute in 23, subacute in 18, and chronic in 33. Clinically, the picture was essentially the same in all three phases of the disease. Hypertension was present in 50%, oedema in 62%, and severe nitrogen retention in 74%. In only 55% of the patients was glomerulonephritis diagnosed before death. It was difficult to determine the actual time of onset of the disease, but there was an average interval of 5·9 years between the onset of recorded symptoms and the last admission to hospital. The authors point out that this may well have been an unreliable figure, since an exacerbation of pre-existing disease might have been recorded as a first attack.

It should be noted that in 45% of the cases there was histological evidence of some other concurrent renal disease besides glomerulonephritis.

C. Bruce Perry

693. **Systemic Capillary Pressure in Acute Glomerulonephritis Estimated by Direct Micropuncture**
M. Macleod. *Clinical Science* [*Clin. Sci.*] **19**, 27–33, Feb. [received April], 1960. 1 fig., bibliography.

The author of this paper from the Department of Medicine, University of Aberdeen, studied the systemic capillary pressure in 7 patients with acute glomerulonephritis, using for this purpose the direct micropuncture method originally described by Landis (*Heart*, 1930, **15**, 209) in which the pressure is measured at the summit of a capillary loop in the skin of the nail fold. In the acute phase the capillary pressure varied from 28 to 41 mm. Hg (three readings being made on each patient); the range in 14 healthy subjects was 16 to 27 mm. Hg. In one patient who died within 6 months of the onset of the illness the capillary pressure 12 weeks after the onset was still raised. In the remaining 6 the pressure after recovery ranged from 16 to 22 mm. Hg. It is suggested that a rapid rise in capillary pressure is a factor in the aetiology of oedema in acute glomerulonephritis and that this rise may be due to fluid retention and hydraemia.

C. Bruce Perry

694. **Viral Nephritis.** (Les néphrites virales)
P. Michon, A. Larcan, F. Streiff, C. Huriet, and X. Berthier. *Presse médicale* [*Presse méd.*] **68**, 309–312, Feb. 20, 1960. Bibliography.

This paper from the Faculty of Medicine of Nancy describes 7 cases of acute nephritis in which examination of throat swabs and serological tests failed to incriminate the streptococcus and in which evidence of viral infection was obtained; in 3 cases the causal organism was the influenza virus, in 2 a rickettsia, in one a neorickettsia (X 14), and in the seventh a virus of the ornithosis–psittacosis group.

The nephritis varied in its severity and there was not always a clear interval between the initial infection and the renal involvement. It is therefore suggested that these cases were probably due to a nephrotropic action of the virus rather than to allergic mechanisms. On the basis of their own findings and of a survey of the literature the authors state that subacute or chronic nephritis practically never follows viral nephritis.

Epidemics of acute nephritis may occur during epidemics of virus infections, but even in sporadic nephritis it is worth while trying to establish the aetiology by bacteriological and serological means. It is thought that in this way the viruses may well be incriminated more and more frequently as the cause of outbreaks of acute nephritis. *T. B. Begg*

Endocrinology

695. **Urinary Sodium Retention after ACTH Stimulation: a Rapid, Simple Screening Test for Adrenal Cortical Insufficiency**
T. M. BATCHELOR and R. E. MOSHER. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **239**, 175–180, Feb., 1960. 2 figs., 18 refs.

The rapid screening test for adrenocortical insufficiency described in this paper from Providence Hospital, Detroit, depends on the changes in the concentration of sodium in the urine 4 hours after an injection of 25 units of ACTH (corticotrophin), a reduction of 50% or more in this concentration being indicative of sodium retention and thus of a responsive adrenal cortex. Several illustrative cases are described. The authors conclude that although the test does not necessarily reflect the over-all integrity of the complex functions of the adrenal cortex, it does measure changes in mineralocorticoid activity, probably of the 11–17-oxysteroids, and point out that it is mainly this mineralocorticoid deficiency which produces the serious clinical problems of adrenal insufficiency. *A. Gordon Beckett*

696. **Aldosterone Excretion in Hypopituitarism and after Hypophysectomy in Man**
E. J. ROSS, W. VAN'T HOFF, J. CRABBÉ, and G. W. THORN. *American Journal of Medicine* [*Amer. J. Med.*] **28**, 229–238, Feb., 1960. 7 figs., 39 refs.

A considerable amount of evidence has been accumulated that in animals the zona glomerulosa, the region of the adrenal cortex responsible for the production of the sodium-retaining hormone aldosterone, is independent of pituitary control. This is supported by the fact that the urinary output of aldosterone by patients with hypopituitarism or after hypophysectomy has been found to be normal or near normal. There are, however, conflicting reports in the literature as to the effect of the administration of corticotrophin on the production of this factor.

The authors of this paper from the Peter Bent Brigham Hospital and Harvard Medical School, Boston, present further observations on the urinary excretion of aldosterone in hypopituitarism and after removal of the hypophysis. Aldosterone was estimated by the physicochemical method of Neher and Wettstein as modified by Hernando *et al.* (*Metabolism*, 1957, **6**, 518). Nine patients with hypopituitarism were investigated while receiving a normal intake of sodium and 3 of them also during salt restriction. Aldosterone output was below normal in all cases and did not increase greatly when a low-salt diet was given, the normal response to this stimulus thus being diminished. Aldosterone excretion was also measured in 4 patients before and immediately after hypophysectomy (for carcinoma of the breast), and was observed to increase considerably in association with the increase in the volume of urine. This relationship between urine volume and aldosterone output was again noticed when vasopressin therapy was withdrawn in one case, and a great increase in aldosterone excretion followed.

It is concluded that these results indicate that while the pituitary is not the major regulator of aldosterone production, it has some influence, perhaps by maintaining the size of the adrenal glands. *Nancy Gough*

THYROID GLAND

697. **Human Auto-immune Thyroiditis: Clinical Studies**
D. DONIACH, R. V. HUDSON, and I. M. ROITT. *British Medical Journal* [*Brit. med. J.*] **1**, 365–373 Feb. 6, 1960. 2 figs., 48 refs.

Since their original demonstration of the existence of thyroid antibodies in Hashimoto's disease (Roitt *et al.*, *Lancet*, 1956, **2**, 820) the authors, working at the Middlesex Hospital, London, have tested for these antibodies in all cases of thyroid disease seen at their clinic. The present paper is primarily devoted to a summary of the clinical aspects of auto-immune thyroiditis. First, however, they review the results of precipitin, tanned erythrocyte-agglutination, and complement-fixation tests for the presence of these antibodies in 636 patients with various forms of thyroid disease. Antibodies were identified by one or more of these tests in 98% of the patients with untreated Hashimoto's disease and in 83% of cases of " primary " myxoedema. Antibodies were also found to be present, although in much lower concentrations, in 67, 33, and 29% of patients with hyperthyroidism, nodular colloid goitre, and thyroid cancer respectively, and in 6% of control subjects. The precipitin test very rarely gave a positive result except in lymphadenoid goitre and primary myxoedema.

From the results of these and other similar published studies the authors conclude that " primary " myxoedema is probably a variant of auto-immune thyroiditis, differing only in the absence of goitre formation. They cite the cases of 2 patients with myxoedema, without palpable thyroid tissue and with antibodies in the serum, in whom a goitre had been present at clinical examination some years previously. Spontaneous resolution of the goitre and the subsequent development of myxoedema due to auto-immunizing thyroiditis occurs similarly, and perhaps more frequently, in hyperthyroidism. The authors also cite examples of Hashimoto's disease which at first resemble cases of de Quervain's subacute thyroiditis, but which often show, as well as the histological difference, a clinical distinction in that permanent hypothryoidism results. Two patients in whom auto-immune thyroiditis was accompanied by hepatitis and by positive results to

tests for complement-fixing antibodies to human liver are also mentioned; in one of them L.E. cells were also present.

The level of antibody titre was low in several cases during the period when the lymphadenoid goitre was developing, but later rose. It seems likely, therefore, that the antibodies so far recognized are the result rather than the cause of the primary lesion in Hashimoto's disease. *H.-J. B. Galbraith*

698. **A Clinical Method of Assessing the Results of Therapy in Thyrotoxicosis**

J. CROOKS, E. J. WAYNE, and R. A. ROBB. *Lancet* [*Lancet*] **1**, 397–401, Feb. 20, 1960. 3 figs., 8 refs.

The authors consider that the present methods available for assessment of the response to treatment in thyrotoxicosis are unsatisfactory and in this paper from the University of Glasgow suggest a new way of approaching this problem. It consists essentially in allocating a numerical value to each clinical sign and symptom of thyrotoxicosis on the basis of its diagnostic significance. By adding the values obtained before starting treatment a total score or " therapy index " is obtained for each patient, and this total score is re-estimated weekly during treatment. Particular importance is attached to increase in appetite and gain in weight, one point being deducted for each 4 lb. (1·8 kg.) gained. Complete remission is taken to have occurred when the therapy index reaches and remains within the range of 0 to 5 for 3 successive weeks.

The method was compared with the results of estimating the basal metabolic rate (B.M.R.) at 2-weekly intervals in two groups each of 20 patients, one group receiving methylthiouracil, 600 mg. daily for 2 weeks followed by 300 mg. daily, and the other potassium perchlorate, 600 mg. a day. In 33 of the 40 patients the fall in the therapy index was linear with time and showed good correlation with the B.M.R. estimations. The results obtained appeared to indicate that methylthiouracil was a more effective drug than potassium perchlorate in the dosage employed, the mean time for complete remission with the former being 9·1 weeks compared with 13·1 weeks for potassium perchlorate. " Cross-over " tests on 14 patients confirmed these findings. The time taken to achieve complete remission was uninfluenced by the initial severity of the disease. *D. G. Adamson*

699. **A Comparison of Potassium Perchlorate, Methylthiouracil, and Carbimazole in the Treatment of Thyrotoxicosis**

J. CROOKS and E. J. WAYNE. *Lancet* [*Lancet*] **1**, 401–404, Feb. 20, 1960. 16 refs.

Employing the " therapy index " described above [see Abstract 698] to assess the response to treatment the authors have compared the relative efficacy of potassium perchlorate in a dosage of 200 mg. 5 times daily (total 1,000 mg.) and carbimazole 20 mg. 3 times daily (total 60 mg.) in two groups each of 20 patients suffering from classic Graves's disease. Combining the results of the two studies they show that methylthiouracil in doses of 600 mg. daily for 2 weeks followed by 300 mg. daily and potassium perchlorate in a dosage of 1,000 mg. daily were almost equally effective as measured by the time taken to produce complete remission (9·1 and 9·4 weeks respectively), while both drugs were more effective than carbimazole in one-tenth of the dose, that is, 60 mg. daily.

In a large series of 486 patients studied over a sufficiently long period it was concluded that potassium perchlorate in doses of 1,000 mg. or less per day was less likely to produce sensitization reactions such as rashes or blood dyscrasias than the organic antithyroid drugs, which behaved similarly in this respect. Higher doses of perchlorate were, however, just as liable to produce toxic effects as the organic compounds, and in one patient treated with 1,500 mg. of potassium perchlorate daily agranulocytosis occurred, the total polymorphonuclear leucocyte count being only 750 per c.mm. On withdrawal of the drug the count rapidly returned to normal levels. In the dosage employed there was no need to restrict dietary iodine during treatment with potassium perchlorate. It was also found to be a suitable drug for treatment of thyrotoxicosis complicating pregnancy and for preoperative preparation.

The authors conclude that potassium perchlorate is the antithyroid drug of choice. *D. G. Adamson*

700. **The Effects of Certain Physical and Emotional Tensions and Strains on Fluctuations in the Level of Serum Protein-bound Iodine**

R. VOLPÉ, J. VALE, and M. W. JOHNSTON. *Journal of Clinical Endocrinology and Metabolism* [*J. clin. Endocr.*] **20**, 415–428, March, 1960. 29 refs.

The effect of physical and emotional tensions and strains on the fluctuation of the serum protein-bound iodine level was studied in groups of healthy people and in two groups of patients. The effect of the tension and strain of examination was observed in 11 medical students preparing for annual examinations and in 11 Royal College of Physicians candidates. The stress of athletic contest on the protein-bound iodine level was observed in 7 professional football players in training and during their scheduled games. There was no fluctuation beyond that found in normal healthy persons. Similarly, in 8 patients prior to and following major operations and in 9 patients following myocardial infarction, the fluctuations of the serum protein-bound iodine level remained within the usual normal range. Our data fail to provide any evidence that the function of the normal thyroid gland is readily affected by severe mental and physical stresses or strains.—[Authors' abstract.]

701. **The Pulmonary Abnormalities in Myxedema**

W. R. WILSON and G. N. BEDELL. *Journal of Clinical Investigation* [*J. clin. Invest.*] **39**, 42–55, Jan., 1960. 31 refs.

The authors report from the College of Medicine, State University of Iowa, Iowa City, the results of a study of pulmonary function in 26 patients with untreated myxoedema, of whom 21 were again studied after receiving thyroid therapy. Of these 26 patients, 16 had myxoedema but no clinical evidence of lung disease, 6 had myxoedema

and extreme obesity, and 4 myxoedema and pulmonary disease, in the form of pneumonia in one case, pulmonary oedema secondary to heart disease in 2, and emphysema in the 4th.

In the patients with uncomplicated myxoedema the vital capacity was essentially normal. In those with obesity as a complication, however, there was moderate reduction in inspiratory capacity, expiratory reserve volume, vital capacity, residual volume, and total lung capacity. Since in such patients the reduced lung volumes return to normal as weight is lost, it is thought that when obesity and myxoedema co-exist the reduction in the volume of the lungs is secondary to the obesity. Myxoedema produced no upset of ventilation, but in 4 out of 6 of the obese patients with myxoedema alveolar hypoventilation was manifested by an increase in arterial pCO_2 and low alveolar ventilation, a process which was found to be reversible with treatment. Since pulmonary disease and abnormality of the bony thorax were excluded in these cases the authors suggest that the muscles of respiration or the neuromuscular coordination were impaired. Patients with myxoedema alone had initially reduced maximal breathing capacity which, however, increased significantly following therapy, suggesting that the " muscular " lesion is reversible. Both the obese and non-obese patients with no lung disease showed a diminished diffusing capacity of the lung for carbon monoxide (DL_{CO}), which increased significantly after treatment. Since it is known that in uncomplicated obesity the DL_{CO} is normal it is suggested that the lowered diffusion is due to changes in the capillaries of the lung produced by myxoedema. It is not known whether this change consists in a reduction in the total number of capillaries, a thickening of the alveolar capillary membrane, or both.

Fully detailed results for all 26 patients are tabulated [but those for the 4 with pulmonary disease are not commented upon]. *D. G. Adamson*

DIABETES MELLITUS

702. Retinopathy and Nephropathy in Diabetes Mellitus: Comparison of the Effects of Two Forms of Treatment

S. Johnsson. *Diabetes* [*Diabetes*] **9**, 1–8, Jan.–Feb., 1960. 27 refs.

About 1940 a change was made in the methods of treatment of diabetics at Allmänna Sjukhuset, Malmö (University of Lund), Sweden. Before this time great emphasis had been laid on the importance of maintaining the urine free from sugar, this being achieved by considerable carbohydrate restriction and frequent doses of soluble insulin—at the expense of a very high incidence of hypoglycaemic reactions. During the past 20 years, however, a more liberal policy has been followed, freedom from polyuria and ketonuria being the main criteria of satisfactory control. This report analyses the histories and, in most cases, the present ophthalmoscopic and urinary findings in 159 diabetics who were under the age of 40 at the onset; in one-third (Group 1) the disease had been diagnosed between the years 1922 and 1935. Patients dying within 5 years of diagnosis in whom proteinuria was not found were excluded. Strict control had been practised in this group (numbering 54 patients) for a total period equivalent to over four-fifths of the total duration of diabetes. For an approximately similar period the treatment of the 105 diabetics diagnosed in the subsequent 10 years (Group 2) had been based on an unrestricted diet and long-acting insulin preparations.

The incidence of proteinuria (nephropathy) in Group 1 was 32%, whereas in Group 2, in which moreover the average duration of the disease was 8·6 years shorter, the incidence was 54%. If only patients who had had diabetes for at least 15 years or who had died earlier with proteinuria were considered the disparity in incidence between the two groups was much greater (9% and 61% respectively). The incidence of severe retinopathy was also much higher in Group 2 (although it is pointed out that the results of the latter study had to be restricted to the patients still living, since the adequacy of the ophthalmoscopic examination of those dying earlier could not be relied on). While appreciating that the experimental conditions in this originally unplanned clinical investigation were not ideal, the author suggests that the results support the view that good control of diabetes delays the development of the late manifestations of the disease. *H.-J. B. Galbraith*

703. Retinal Capillary Microaneurysms: a Concept of Pathogenesis

C. H. Pope Jr. *Diabetes* [*Diabetes*] **9**, 9–13, Jan.–Feb., 1960. 9 figs., 16 refs.

In the Department of Pathology, Washington University, St. Louis, the retinae obtained at necropsy from 4 diabetic patients and from 4 patients without a personal or family history of diabetes have been compared, a large variety of routine histological stains and methods being used. The retinae from the diabetics showed abnormal deposits of stained fat in the walls of the capillaries, these deposits being situated in unusually large, but otherwise natural, spaces between the layers of the basement membrane and occasionally within the endothelial cells. In more advanced lesions the basement membrane was thickened by obliteration of these spaces. Micro-aneurysms lacked the reticulum layer which lies external to the basement membrane of the capillaries of normal retinae and which is present in the wall of the capillary adjacent to the micro-aneurysm.

Hitherto it has been suggested and accepted that diabetic micro-aneurysms form as a result of elongation of capillaries with the formation of loops, the adjacent walls of which fuse. The present author points out, however, that in this case the normal reticulum layer should still be found on the outer surface of these lesions. In fact this layer was absent from every microaneurysm he examined. Furthermore the angle between the outer wall of the aneurysm and the wall of the capillary from which it arises was invariably acute, and not obtuse as would be expected on the suggested theory. An alternative hypothesis based on the present findings is therefore proposed, namely, that the micro-aneurysm is a sequel

to an accumulation of fat in the capillary wall, this deposit extending into the reticular layer and separating its fibres. The remaining structures of the capillary wall then herniate through the defect in the supporting network. The fatty deposit is presumably related to the increase in the serum lipid content which occurs in diabetics and especially those with retinopathy. The localization of the lesions to the venous end of the capillaries is perhaps the result of a local increase in endovascular pressure. *H.-J. B. Galbraith*

704. **The Skin-surface-glucose Test: an Aid in the Diagnosis of Diabetes Mellitus**
D. I. MILLER and A. S. RIDOLFO. *Diabetes* [*Diabetes*] **9**, 48–52, Jan.–Feb., 1960. 3 figs., 11 refs.

Since some of their diabetic patients using glucose oxidase test papers (" tes-tape ") to detect the presence of glycosuria had reported that positive results were shown by strips held in the fingers, even although contamination of the skin had been avoided, the authors, working at Marion County General Hospital, Indianapolis, and the Lilly Research Laboratories, have compared the results of synchronous skin, urine, and blood tests for sugar in 86 diabetics and in 64 non-diabetic control subjects.

In a group of ambulant diabetic patients the reaction of moistened test paper held between the fingers was frequently positive, but there was no correlation between a positive result and the urinary and blood glucose level. In 2 diabetics who were studied in greater detail in hospital it was noted that when they were receiving a high-carbohydrate diet the skin test results were consistently positive. Positive results were obtained less frequently when the carbohydrate intake was reduced with, in consequence, a decrease in the blood sugar level. Of the 64 control subjects, who were thought to be non-diabetic, 11 showed positive skin tests but no glycosuria or hyperglycaemia. However, 9 of these 11 subjects gave a diabetic response to glucose tolerance tests or to cortisone–glucose tolerance tests. In a few instances the strip gave a positive reaction when held in the fingers of one hand of a diabetic but not when held in the other hand.

The authors conclude that a positive skin test probably indicates that the blood sugar level is, or has recently been, raised, and suggest that this simple technique may be of value as an additional screening test for diabetes when community surveys are being undertaken.

H.-J. B. Galbraith

705. **Application of the Double Intravenous Glucose Tolerance Test to the Study of Diabetes.** (Application de la double épreuve d'hyperglycémie intraveineuse à l'étude du diabète)
T. RODARI and G. SPECCHIA. *Acta endocrinologica* [*Acta endocr.* (*Kbh.*)] **33**, 157–167, Feb., 1960. 1 fig., 37 refs.

The authors of this paper from the University of Pavia, Italy, report the results of performing the double intravenous glucose test on 37 diabetics. It was found that these patients could be divided into three main clinical groups, namely, obese diabetics with no acidosis, thin diabetics with a tendency to acidosis, and a small group of intermediate classification. There was a difference between the " coefficient of glucose assimilation " after the second intravenous injection of glucose in the obese diabetic group, whereas there was no difference between the results of the first and second injections in the thin diabetics and the intermediate group. The authors conclude that the double intravenous glucose test provides physiological proof of the clinical differentiation into obese diabetics and thin diabetics.

I. McLean Baird

706. **Incidence of Diabetes Mellitus in the Butha-Buthe District of Basutoland**
W. M. POLITZER, B. HARDEGGER, and T. SCHNEIDER. *British Medical Journal* [*Brit. med. J.*] **1**, 615–617, Feb. 27, 1960. 27 refs.

Seven cases of diabetes mellitus were found among 3,000 Basuto in the Butha-Buthe district of Basutoland during an investigation into the incidence of glycosuria. This represents an incidence of 0·23%. The " tes-tape " method was used and 12 cases of glycosuria were discovered in all. In 7 of these the venous blood glucose level was found to be above 140 mg. per 100 ml. These findings are discussed in the light of a similar study carried out in the U.S.A., where the incidence of diabetes mellitus is 1·7% of the population. It is suggested that a low incidence of diabetes in a primitive community is associated with a low-calorie diet consisting mainly of carbohydrates. *A. I. Suchett-Kaye*

707. **Asymptomatic Bacilluria in Sixty-eight Diabetic Patients**
R. T. RENGARTS. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **239**, 159–164, Feb., 1960. 10 refs.

This paper from the Joslin Clinic and New England Deaconess Hospital, Boston, describes the findings in 68 diabetic patients, 46 of them women, who had bacilluria without clinical evidence of genito-urinary disease. Of the 23, of whom 19 were women, with the most severe grades of bacilluria (more than 100,000 organisms per ml.), 17 (68%) had been confined to bed for some time before the test, only 5 were hypertensive, and 8 had poorly controlled diabetes. Although the majority had proteinuria, the finding of leucocytes in the urine was unreliable in the prediction of bacilluria. The commonest organisms present were *Escherichia coli*, *Bacillus proteus*, *Staphylococcus albus*, and *Aerobacter* spp. *A. Gordon Beckett*

708. **Amelioration of Human Hypoglycemic Symptoms by Intravenous Fructose**
H. S. SELTZER, M. IUNES, E. J. KULINSKI, and J. W. CONN. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **239**, 213–220, Feb., 1960. 2 figs., 26 refs.

Working at the University of Michigan Medical School, Ann Arbor, the authors have studied in 7 healthy young subjects (one female) the effects of fructose

in relieving hypoglycaemia during intravenous insulin tolerance tests. First a baseline insulin tolerance test was performed. Next day, using larger doses of insulin to produce comparably low blood sugar levels, the test was repeated after an intravenous drip of fructose had been running for 90 minutes at the rate of 1 g. of fructose per kg. body weight per hour. The symptoms of hypoglycaemia in all the subjects were now considerably less severe or of shorter duration. It was demonstrated, however, that administration of fructose had no effect in relieving hypoglycaemic symptoms once these were established. The changes in the number of circulating eosinophils, measured during the tests as representing the levels of circulating adrenaline, showed that the intensity of hypoglycaemic symptoms was related to the magnitude of the adrenaline response. A very much smaller rise in the eosinophil count was obtained during fructose infusion.

The authors consider that the partially protective action of fructose is mediated principally by its effect in increasing hepatic gluconeogenesis, with a resulting replenishment of circulating glucose. As only a small fraction of infused fructose is converted into glucose, however, its value is limited. They conclude therefore that the protective effect of fructose is quantitatively small and of no clinical application, and that thus the infusion of fructose during the treatment of diabetic coma is not a reliable buffer against hypoglycaemia.

A. Gordon Beckett

709. **Comparison of Acute Hypoglycemic Potencies of Tolbutamide and Chlorpropamide**

J. W. Craig, M. Miller, F. D. Mills, and N. Nickerson. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **172**, 779–782, Feb. 20, 1960. 1 fig., 13 refs.

In experiments reported from Western Reserve University School of Medicine, Cleveland, tolbutamide and chlorpropamide were given intravenously to diabetic subjects and their effects on the blood sugar level compared. The subjects were 21 patients with stable diabetes, each patient being tested at least twice, once with tolbutamide and on another occasion with an equal dose of chlorpropamide. Doses of 1·0, 0·5, 0·25, and 0·125 g. of the sodium salts of the compounds were used. The blood glucose level was determined at 30-minute intervals for 3 hours. At all four dose levels equal quantities of tolbutamide and chlorpropamide produced similar decreases in the blood glucose concentration during the 3 hours after administration. Determinations of the plasma concentrations of the two drugs showed little difference between them, though the average tolbutamide level was usually slightly less than that of chlorpropamide after 2 and 3 hours.

It is concluded from these results and from longer-term studies by other investigators that the two compounds probably do not differ in their intrinsic hypoglycaemic potencies, the smaller dosage requirement of chlorpropamide being explained by the higher serum level achieved owing to a slower rate of inactivation and excretion.

K. O. Black

710. **An Effect of Tolbutamide on Ketogenesis, *in vivo* and *in vitro***

B. R. Boshell, G. R. Zahnd, and A. E. Renold. *Metabolism: Clinical and Experimental* [*Metabolism*] **9**, 21–29, Jan., 1960. 3 figs., 25 refs.

The administration of 3 g. of tolbutamide by mouth to 6 fasting, untreated, tolbutamide-responsive diabetics at the Peter Bent Brigham Hospital (Harvard Medical School), Boston, resulted in a 50% fall in blood glucose and ketone body levels. Incubation of liver slices from fasted rats with 1 and 0·2 mg. of tolbutamide per ml. resulted in 62% and 30% inhibition of ketogenesis respectively, while incubation with 0·1 unit of insulin per ml. caused no significant depression. Incubation of such slices with 1 mg. of tolbutamide per ml. in the presence of acetate resulted in 36% inhibition of ketogenesis. Tolbutamide (1 mg. per ml.) produced a 25% fall in ketogenesis by human liver slices obtained at operation from non-fasting patients, and similar concentrations of tolbutamide induced a large inhibition of ketogenesis in liver slices from alloxan-diabetic and pancreatectomized rats. These results indicate that in addition to its recognized effects on the pancreas tolbutamide exerts an effect upon liver tissue not mediated by insulin.

F. W. Chattaway

711. **Treatment of Diabetes with Metahexamide**

R. H. Pollen, R. H. Barnes, D. C. Tanner, W. H. Stimson, and R. H. Williams. *Diabetes* [*Diabetes*] **9**, 25–30, Jan.–Feb., 1960. 16 refs.

The authors, from the University of Washington School of Medicine, Seattle, report the use of metahexamide, an oral sulphonylurea, in the treatment of 92 diabetic patients. Those patients who failed to respond to the average daily dose of 100 mg. rarely responded to larger amounts.

The effect of treatment was satisfactory in 39 cases, as judged by a fasting blood sugar level of under 130 mg. per 100 ml., or by a blood sugar level 2 hours after a meal of less than 150 mg. per 100 ml. Fair results were obtained in a further 10, but in the remaining 43 patients the treatment was considered to have failed. The patients who were benefited included some who had previously failed to respond, or failed to maintain their response, to tolbutamide or chlorpropamide. Of 18 patients whose disease had appeared before the age of 40 years, 16 did not benefit from metahexamide.

Definite or possible undesirable reactions to the drug occurred in 11 of those who received more than a single dose and were severe enough to require termination of treatment in 5. Gastro-intestinal disturbances, malaise, and symptomless hepatic dysfunction (indicated by increased retention of "bromsulphalein") were the most common side-effects. In view of these findings and of reports from other workers of severe hepatotoxic effects of the drug the present study is not being extended. The authors suggest that, were it not for this possibly dangerous reaction, metahexamide would be of value in those diabetics who, although apparently suitable for sulphonylurea therapy, do not respond to tolbutamide.

H.-J. B. Galbraith

The Rheumatic Diseases

712. **The Significance of Blood Serum Glycoprotein Estimations in the Evaluation of the Activity of a Rheumatic Process.** (Значение исследования гликопротеидов сыворотки крови для выявления активности ревматического процесса)
O. L. Duhovnaja. *Терапевтический Архив* [*Ter. Arh.*] **32**, 10–15, Feb., 1960. 2 figs., 26 refs.

The author reports the results of an electrophoretic study of the serum glycoproteins in 120 rheumatic patients and 33 healthy control subjects. In the controls glycoproteins were present in all plasma protein fractions, the highest content being in the α_2 globulins. In patients with active rheumatism the glycoprotein content in both the α_1- and α_2-globulin fractions was higher than in the controls, but in the albumin and β- and γ-globulin fractions it was considerably lower. With the subsidence of rheumatic activity the proportions moved towards normal. These changes were more evident in the glycoproteins than in the protein fractions themselves, and this method is therefore regarded as being more sensitive for the detection of activity of a clinically inactive rheumatic process.

[A similar communication by Denisova in the same issue reports much the same findings, except that in some 33% of her active cases of rheumatism the γ-globulin glycoprotein content was also raised. She also reports a certain parallelism between the glycidogram and the proteinogram, but in 10% of her patients the latter remained normal, whereas the former revealed changes and is therefore considered to be more reliable.]

L. Firman-Edwards

713. **The Clinical Picture of Rheumatic Thrombovasculitis.** (Клиника ревматических тромбоваскулитов)
G. L. Hasis and E. S. Sigal. *Терапевтический Архив* [*Ter. Arh.*] **32**, 24–30, Feb., 1960. 14 refs.

The authors describe 16 cases of rheumatic thrombovasculitis occurring in 8 male and 8 female patients ranging in age from 14 to 56 years, several of whom had more than one attack. The vessels involved were the cerebral arteries in 13 cases, the limb arteries in 3, the pulmonary in 3, the cardiac in 2, the renal in 2, and the intestinal in one. Three of the attacks took place during the first bout of acute rheumatism, 9 during subsequent attacks, and the others during intervals between bouts. The outcome was satisfactory in 13 cases, but proved fatal in 3. Case histories of 3 of the patients are given, including 2 of those who died and came to necropsy. All the 16 patients had cardiac lesions.

The authors state that the condition is much commoner than is realized and may often remain undiagnosed, especially in the milder, latent forms. Histologically, the lesions consist of lymphoid infiltration of the arterial walls (granular leucocytes are also often found), with thickening of the walls and clot formation in the lumen. In one of the fatal cases thrombosis of the abdominal aorta with gangrene of the left leg is described. They suggest that this complication of rheumatism deserves further investigation.

L. Firman-Edwards

RHEUMATIC FEVER

714. ***beta*-Hemolytic Streptococci and Rheumatic Fever in Miami, Florida. II. Antistreptolysin O Titer Determinations between October 1954 and May 1955**
M. M. Streitfeld and M. S. Saslaw. *Diseases of the Chest* [*Dis. Chest*] **37**, 211–221, Feb., 1960. 16 refs.

An investigation is reported from the University of Miami School of Medicine, Florida, of the antistreptolysin-O titre in serial blood samples obtained from 236 school children during the winter of 1954–5. Blood was drawn in all cases at the beginning and end of the study. Throat swabs were obtained as a routine each month, and whenever β-haemolytic streptococci were cultured blood samples were withdrawn more frequently. In 48 out of a total of 472 blood samples the antistreptolysin-O titre was 250 or higher. The lowest average initial and final titres were found in children from whom no streptococci or only Group-B organisms were isolated and the highest in those with Group-A organisms. Infections by streptococci of Groups C and G were accompanied by moderate increases in titre. A rising antistreptolysin-O titre in successive blood samples was observed in 16 (29%) out of 55 children with typable Group-A strains, 9 (27%) of 37 with non-typable Group-A strains, 3 (17%) of 18 with Group-C organisms, and 10 (9%) of 99 with negative throat swabs. Between 1953 and 1955 a general rise in antistreptolysin-O titre was observed among those children for whom data were available over the 2-year period. There were 57 incidents of Group-A streptococcal infection associated with a 2-tube rise in antistreptolysin-O titre, but none of the affected children developed rheumatic fever. The authors emphasize that the value of isolated and serial estimations of antistreptolysin-O titre is limited and requires careful assessment.

Allan St. J. Dixon

715. **Comparison of the Recurrence Rate of Rheumatic Carditis among Children Receiving Penicillin by Mouth Prophylactically or on Indication**
W. N. Lim and M. G. Wilson. *New England Journal of Medicine* [*New Engl. J. Med.*] **262**, 321–325, Feb. 18, 1960. 16 refs.

The difficulty of maintaining continuous chemoprophylaxis with penicillin in children with a past history of rheumatic fever, together with certain theoretical considerations, led the authors to investigate the value of such prophylaxis compared with that of penicillin treatment given on clinical indication alone. The study

was made over a 6-year period on children who had had at least one observed attack of rheumatic carditis and were attending the Cardiac Rheumatic Clinic of the New York Hospital, 110 of whom received continuous prophylaxis (Group 1) and 103 received penicillin therapy for 10 days only when indicated by the onset of a respiratory infection or signs of faucial inflammation (Group 2). The selection of the groups was not made at random, children with recent carditis usually being given continuous prophalaxis, while transfers from one group to the other also occurred. Group 2 contained a higher proportion of older children (13 to 16 years) than Group 1.

The recurrence rate of rheumatic carditis was found to be 6·6 per 1,000 patient-months in Group 1 and 2·9 per 1,000 in Group 2. This difference was found to be due to the greater number of more susceptible children with recent attacks in Group 1. There was no significant difference between the recurrence rates in different age groups in either group. Altogether 17 recurrences were observed in Group 1 (associated with chorea in 7 cases and polyarthritis in 9) and 8 in Group 2 (with chorea in 3 cases and polyarthritis in 5). Spot throat cultures in Group 1 revealed the presence of β-haemolytic streptococci in 9 of 98 children who had sore throats; none of these relapsed, whereas in throat swabs from 10 children who relapsed no β-haemolytic streptococci were found. In Group 2, of 94 spot cultures from children with sore throats, β-haemolytic streptococci were isolated from 15, while of 6 throat cultures from patients with recurrences, β-haemolytic streptococci were isolated from 5.

Although it is agreed that there has been a great decline in the incidence of rheumatic fever in recent years, the authors point out that this decline antedated the antibiotic era and has not been accelerated since. They conclude that for children under close medical supervision continuous oral penicillin prophylaxis has no advantage over adequate penicillin therapy as indicated. Indeed it remains possible that the recurrence rate in this trial would have been the same if no penicillin had been given at all.

[This is a challenging paper. Nevertheless, the authors' conclusions should not be accepted without fuller proof. The two groups were not comparable, and subclinical streptococcal infections were not looked for by estimation of the antistreptolysin-O titre. It is of interest that β-haemolytic streptococci were isolated from 9 children receiving continuous prophylaxis, none of whom developed rheumatic fever, whereas of 15 children in Group 2 from whom β-haemolytic streptococci were isolated, 8 suffered a recurrence of their rheumatic carditis.] *John Lorber*

716. **Studies of Blood Lipid Fractions of Quiescent Rheumatic Fever Patients and Their Siblings**
H. D. Appleton, A. F. Coburn, and Y. L. Meltzer. *Clinical Chemistry* [*Clin. Chem.*] **5**, 557–565, Dec., 1959. 13 refs.

It has been claimed that in rheumatic fever the fasting serum level of lipoprotein streptolysin-S inhibitor is significantly lower than normal, even during the quiescent phase of the disease. This study reported from New York Medical College and Metropolitan Hospital, New York, was designed to determine whether rheumatic fever is associated with abnormalities in the serum lipid level which might be due to genetic or environmental factors. It was found that in rheumatic children under the age of 14 years in whom the disease had been quiescent for one year the mean non-fasting lecithin plasma level (2·76 mMol. per litre) was significantly lower than in their healthy siblings (3·15 mMol. per litre) living under similar environmental conditions. The part played by constitution, heredity, and the disease in bringing about this difference is unknown [and its significance in aetiology is largely conjectural]. *E. J. Holborow*

717. **Antibody Titers in Acute Rheumatic Fever.** [Review Article]
L. W. Wannamaker and E. M. Ayoub. *Circulation* [*Circulation*] **21**, 598–614, April, 1960. 2 figs., bibliography.

CHRONIC RHEUMATISM

718. **Research on the Behaviour, Nature and Meaning of the Rheumatoid Factor.** [In English]
A. Robecchi and V. Daneo. *Acta rheumatologica Scandinavica* [*Acta rheum. scand.*] **5**, 245–262, 1959 [received March, 1960]. 28 refs.

In the first part of this paper from the Ospedale S. Giovanni Battista, Turin, the results of the Rose–Waaler test carried out on 3,050 occasions on 1,643 subjects, including patients with rheumatoid arthritis and various rheumatic and non-rheumatic diseases and healthy controls, are analysed in some detail. Sensitization of the erythrocytes was " reduced in intensity " in an attempt to increase specificity. With this modification agglutination at a dilution of 1:64 was regarded as a positive reaction.

Of 511 cases of rheumatoid arthritis, 63·9% gave a positive reaction to the test. Further analysis of these results showed that: (1) no patient under the age of 15 years gave a positive response, the highest percentage of positive responses being found in middle age regardless of the duration of the disease; (2) there was no significant difference in the behaviour of the response between the sexes; (3) the proportion of positive results and the height of the titre increased with the duration of the disease, very high titres being found in cases in which a positive response had been obtained early in the disease process; and (4) there was a direct relationship between the intensity of the reaction and the severity of the radiological changes. No clinical difference between cases giving positive and negative reactions could be detected, nor was any alteration observed which could be attributed to treatment.

The results in numerous other pathological conditions are also reported [and are generally concordant with those of other authors]. In a control group of 628 subjects (which included cases of osteoarthritis and periarthritis)

false positive results were obtained in 0·63%. High agglutinating titres were found in 2 out of 23 cases of pulmonary silicosis. In a group of 99 cases of wholly non-rheumatic disease only 2 positive reactions were obtained. Relatives of patients with rheumatoid arthritis gave a positive reaction in 27·3% of cases compared with 8% in a control group. Comparison of the Rose–Waaler test with the Hyland drop latex test showed correlation in 82·7% of cases. However, this latex procedure gave 14·5% false positive results compared with 0·77% with the Rose–Waaler test.

The second part of the paper deals with various investigations directed towards the elucidation of the nature of this phenomenon. Eradication of any one of the four portions of complement did not remove the agglutinating capacity of serum. No success was obtained in the determination of a precipitation reaction. The authors found no evidence of hypersensitivity or immunization to heterologous globulins. The agglutinating factor was found in joint fluid and in the interstitial fluid. *Harry Coke*

719. **Persistence of Intra-articular Steroid: Experience with Prednisolone Trimethylacetate**

G. Will and W. R. Murdoch. *British Medical Journal* [*Brit. med. J.*] **1**, 94–95, Jan. 9, 1960. 6 refs.

Experiments were carried out at Glasgow Royal Infirmary designed to determine the relative persistence of certain steroids in the joint cavity following intra-articular injection. Specimens of synovial fluid were obtained from 50 joints (49 knees and one elbow) at intervals after the injection and were then examined chromatographically for the presence of steroid.

In the first experiment prednisolone trimethylacetate was injected into 8 joints and hydrocortisone acetate into 8, the 16 joints being aspirated completely after 24 hours and the fluid examined. Prednisolone was identified in the fluid from all 8 joints into which it was injected, but hydrocortisone was not recovered from any of the joints injected with this steroid. In a further experiment prednisolone was injected into 12 joints, which were aspirated at longer intervals. Prednisolone was present in the fluid up to 6 days after injection of 50 mg. As an extension of this 16 further joints were injected and the fluid examined 7 days later; prednisolone was not usually present when the original dose was below 50 mg.

Finally, 5 joints were aspirated 10 or 14 days after injection of 60 to 100 mg. of prednisolone. Of 3 joints aspirated 10 days after injection, 2 contained steroid; there was no steroid in the fluid from 2 joints aspirated after 14 days. The steroid was detected in an elbow joint after 14 days, although the dose had been only 25 mg.

The rapid disappearance of hydrocortisone from the joint cavity confirms the findings of previous workers. Prednisolone detected in joint fluid was usually the free alcohol, and it is presumably this form which exerts an anti-inflammatory local action, the relatively insoluble trimethylacetate acting merely as a local application.
B. E. W. Mace

720. **Heparin–Latex Test in Rheumatoid and Non-rheumatoid Serums**

G. K. de Forest and J. J. Barboriak. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **103**, 115–117, Jan., 1960. 3 refs.

It has been reported by Gofton *et al.* (*Canad. med. Ass. J.*, 1957, **77**, 1098; *Abstr. Wld Med.*, 1958, **23**, 454) that certain polysaccharides can be used in place of α-globulin to " sensitize " latex particles in the latex fixation test of Plotz and Singer. The present authors, working at Yale University School of Medicine, describe a modified latex fixation test for agglutination in which heparin is used as the heterologous sensitizing agent and which they applied to 90 sera specially selected as likely to give false positive reactions by reason of having a high α-globulin content (over 20% of total protein) as determined by paper electrophoresis. The heparin–latex test gave 52% positive results as against 20% in the standard test, which gave 6·4% false positive results in a series of 313 unselected control sera. The authors conclude that the heparin–latex method offers no improvement in routine tests for rheumatoid arthritis.

[The investigation was undertaken on account of the fact that the definition of " rheumatoid factor " adopted by the Arthritis and Rheumatism Foundation " implies the obligatory presence of an ' outside ' α-globulin in serological reactions in which the rheumatoid factor participates ". It is difficult, however, to determine the source of this obligation in the official definition].
Harry Coke

721. **Clinical Evaluation of Chloroquine in Rheumatoid Arthritis**

S. R. La Tona and B. M. Norcross. *Archives of Interamerican Rheumatology* [*Arch. interamer. Rheum.*] **2**, 595–599, Dec., 1959 [received March, 1960]. 5 refs.

In this paper from the University of Buffalo Medical School, New York, the authors report an uncontrolled trial of chloroquine phosphate in the treatment of 145 unselected patients with rheumatoid arthritis in varying degrees of activity. The usual dosage was 250 to 500 mg. daily, and the duration of the trial was 6 to 18 months. Side-effects occurred in 41 patients, the commonest being nausea, dyspepsia, headache, dizziness, pruritus, and dermatitis; in 13 patients these reactions were severe enough for administration of chloroquine to be stopped. Corneal changes developed in 2 patients. Improvement was noted in only 35 (31%) patients. No correlation was observed between the response to the drug and sex, age, or duration of the disease. *J. A. Cosh*

722. **Some Effects of Ankylosing Spondylitis on Pulmonary Gas Exchange**

A. D. Renzetti Jr., W. Nicholas, R. E. Dutton Jr., and L. Jivoff. *New England Journal of Medicine* [*New Engl. J. Med.*] **262**, 215–218, Feb. 4, 1960. 13 refs.

Pulmonary function was studied in 12 male patients with clinical and radiological evidence of ankylosing spondylitis, but without lung or heart disease. It was found that vital capacity and total lung capacity were

reduced, but the maximum ventilatory capacity and the index of intrapulmonary mixing remained normal. Hyperventilation at rest and during and after exercise was observed in most of the patients, and there was mild arterial oxygen unsaturation in half of them. The percentage venous admixture was increased in 5 of the 6 patients so studied. It is suggested that the hyperventilation and the gas exchange defects might result from relative over-expansion of the lower and under-expansion of the upper portions of the lung. *K. C. Robinson*

GOUTY ARTHRITIS

723. **Clinical Experience with Zoxazolamine as a Uricosuric Agent in Gout**

A. L. KOLODNY. *Journal of Chronic Diseases* [*J. chron. Dis.*] **11**, 64–68, Jan., 1960. 1 fig., 6 refs.

Zoxazolamine is rapidly absorbed and is eliminated from the body in approximately 6 hours. It acts by inhibiting the tubular reabsorption of urates. Over a period of 27 weeks it was given in the treatment of acute, intercritical, and chronic gout in 11 patients (9 male and 2 female). Pronounced uricosuric effects were obtained when a dose of 250 mg. was administered 2 to 4 times daily after meals and at bedtime. As regards diet, neither alcoholic nor purine foods were restricted in quantity. The daily intake of fluids ranged from 2 to 3 litres and when this was maintained it was not necessary to ensure that the urine was alkaline. There was some interference with the uricosuric action of the drug when salicylates were given concomitantly. On the other hand phenylbutazone had an additive effect, as did probenecid though to a lesser extent than phenylbutazone.

In 10 cases the clinical condition was either controlled or improved, but in the remaining case a urinary infection supervened and the patient died from uraemia. A maintenance dosage of 250 mg. twice daily resulted in diminution in the size of tophaceous deposits. Dizziness and nausea were the only recorded side-effects and were usually mild. The onset of nausea could be prevented by giving zoxazolamine during a meal. In 3 patients with renal damage acute attacks of gout developed during the early stages of treatment; these exacerbations subsided promptly following administration of colchicine. In spite of the loss of uric acid in the urine, no uric acid stones were observed. *A. Garland*

724. **Suppression of Uric Acid Synthesis in the Gouty Human by the Use of 6-Diazo-5-oxo-L-norleucine**

A. I. GRAYZEL, J. E. SEEGMILLER, and E. LOVE. *Journal of Clinical Investigation* [*J. clin. Invest.*] **39**, 447–454, March, 1960. 5 figs., 25 refs.

At the National Institute of Arthritis and Metabolic Diseases, Bethesda, Maryland, 6-diazo-5-oxo-L-norleucine (DON) was administered to 6 patients with gout and to one patient with renal urate lithiasis in order to observe its effect on uric acid production. In 3 patients the drug suppressed the incorporation of glycine-1-^{14}C into urinary uric acid. The absorption of glycine-1-^{14}C from the intestine was unaffected by DON, this finding supporting the view that in the dosage used the drug acts primarily by suppression of purine synthesis. Balance studies showed a reduction in serum urate levels and 24-hour urinary uric acid excretion in only 2 of the 7 patients tested. The negative findings in the other 5 may have been due to the short duration of the balance studies and the presence of an expanded urate pool. The main toxic effects of the drug consisted in soreness of the mouth, sometimes with ulceration, and asymptomatic duodenal ulcers which healed promptly on medical treatment. No depression of the formed elements of the blood were seen. The high incidence of side-effects prevents the practical use of this particular compound in practice, but the possibility remains that more specific and less toxic inhibitors of purine biosynthesis may be found. *G. W. Csonka*

COLLAGEN DISEASES

725. **Anti-cytoplasmic Factors in the Sera of Patients with Systemic Lupus Erythematosus and Certain Other Diseases**

H. R. G. DEICHER, H. R. HOLMAN, and H. G. KUNKEL. *Arthritis and Rheumatism* [*Arth. and Rheum.*] **3**, 1–15, Feb., 1960. 1 fig., 42 refs.

This complex study was carried out at the Rockefeller Institute, New York. Using extracts in normal saline of various animal and human organs as antigens the authors demonstrated complement fixation with sera from 33 out of 37 patients with systemic lupus erythematosus (S.L.E.), 7 out of 11 patients with primary biliary cirrhosis, 2 out of 3 patients with Sjögren's syndrome, and one patient with scleroderma. Positive results were also obtained with 8 out of 35 normal sera, but in low titre. Sixteen sera giving positive reactions with saline extracts were then tested against 5 preparations containing isolated calf thymus nuclei, an extract of such nuclei in phosphate buffer, isolated calf liver mitochondria, microsomes, and a soluble cellular fraction respectively. Ten of these sera, from patients with S.L.E., all reacted positively with all 5 cellular preparations. In the case of the mitochondria and microsomes it was possible to exclude contamination with soluble nuclear material as a cause of the positive reactions since complement-fixation tests using the supernatant from the last wash of these constituents as antigen gave a negative result in each case. Of the other 6 sera tested against the cell fractions, 4 were from patients with biliary cirrhosis, one from a patient with discoid L.E., and one from a case of Sjögren's syndrome. With these sera positive results were obtained against mitochondria and microsomes, but the results with the other preparations varied. However, the results with nuclear material always matched those with the soluble cellular fraction. In some cases control tests with 10 normal sera gave low-titre ($<1:16$) positive results against mitochondrial and microsomal preparations only.

Further work with tissue extracts in various solvents and after treatment with certain enzymes suggested that a number of different cytoplasmic constituents were involved in these reactions, but that one of these con-

stituents seemed to react only with S.L.E. sera. Electrophoresis of the test sera on starch medium and zone ultracentrifugation experiments showed that the antibody constituent of these reactions were γ globulins with a sedimentation constant of 7. (Some of the sera from patients with diseases other than S.L.E. contained additional active 19S globulin). *M. Wilkinson*

726. **Hemagglutination Study of Serum Factors Related to L.E. Cell Formation**
R. C. Lee and W. V. Epstein. *Arthritis and Rheumatism* [*Arthr. and Rheum.*] 3, 41–48, Feb., 1960. 1 fig., 29 refs.

In studies carried out at the University of California School of Medicine, San Francisco, L.E. factor was measured by its ability to agglutinate sheep's erythrocytes treated with tannic acid and coated with a nucleoprotein extract from calf thymus. Rheumatoid factor was measured by the agglutination of cells coated with Cohn Fraction II of human plasma.

All sera from 10 cases of systemic lupus erythematosus agglutinated cells coated with nucleoprotein extract in titres up to 1:64,000, but only 4 of the sera agglutinated cells coated with Fraction II. All sera from 10 patients with rheumatoid arthritis gave Fraction-II titres of 1:56,000 or higher, but none produced L.E. cells or agglutinated cells coated with nucleoprotein extract. Previous exposure of the treated cells to γ globulin inhibited Fraction-II haemagglutination, but not nucleoprotein-extract haemagglutination, whereas exposure of the treated cells to nucleoprotein extract inhibited nucleoprotein-extract haemagglutination but not Fraction-II haemagglutination. Deoxyribonucleic acid failed to inhibit nucleoprotein-extract haemagglutination. The formation of L.E. cells was inhibited by nucleoprotein extract, but not by γ globulin.

The authors consider that nucleoprotein-extract haemagglutination gives a quantitative measure of the serum factor responsible for L.E.-cell formation.

M. Wilkinson

727. **The Heart in Systemic Lupus Erythematosus**
W. Brigden, E. G. L. Bywaters, M. H. Lessof, and I. P. Ross. *British Heart Journal* [*Brit. Heart J.*] **22**, 1–16, Jan., 1960. 19 figs., 10 refs.

In the past 10 years the authors have studied, with particular reference to cardiac involvement, 60 patients with systemic lupus erythematosus (S.L.E.) who were seen at the Hammersmith Hospital, the London Hospital, and the Canadian Red Cross Memorial Hospital, Taplow. Clinical details are given, and the non-cardiac manifestations and serological and haematological findings, as well as the post-mortem findings in the 27 patients who died, are described.

Of the latter, endocarditis was found at necropsy in over half, the mitral valve being involved in 10 cases, the aortic valve in 4, and the pulmonary and tricuspid valves once each. The valvular lesion was primary in 13 cases and in 2 there was a secondary superimposed bacterial infection. The primary lesions, which were of a type previously reported in the literature, occur commonly at the base of the valve, particularly in the valve pocket, and numerous endothelial cells, Antischow myocytes, and inflammatory mononuclear cells are present, the disintegration of these resulting in the formation of haematoxylin bodies and eosinophilic fibrinoid material. The myocardial fibres were seldom involved, but in one patient there was patchy degeneration of some fibres, the nuclei of which lost definition and resembled the inclusion body of an L.E. cell. Myocardial fibrosis with associated vascular occlusion was present in 2 patients, but myocardial abnormalities were mostly interstitial and sometimes extensive. A common finding was a fibrinoid lattice with cellular infiltration, many of these cells undergoing degeneration to haematoxylin bodies. In some cases the fibrinoid lattice appeared to have formed on collagenous strands proceeding from an oedematous area of connective tissue. The authors consider that the characteristic fibrinoid change derives mainly from clotting of fibrinogen in areas of gelatinous exudate, but occasionally local cellular infiltration occurs and the products of nuclear degeneration then contribute to the fibrinoid substance, which may thus differ in different diseases and even in different sites in the same organ. The pericardium was abnormal in 20 of the 27 patients coming to necropsy, the layers usually being obliterated. There was much fibrinoid change and many haematoxylin bodies were present.

The incidence of clinical cardiac manifestations is then discussed. Endocarditis is not recognized clinically so often as it is found at necropsy, since the organic murmurs are often soft and transient and the valvular lesion rarely results in significant obstruction or incompetence. The various murmurs elicited are described in detail, together with reproductions of illustrative electro- and phonocardiograms. The aortic and mitral valves were found to be affected far more commonly than the valves of the right heart. Myocarditis was difficult to detect clinically because of its association with pericarditis, hypertension, and possible water retention as a result of corticosteroid therapy. In no case could heart failure be attributed solely to myocarditis. In the authors' experience pericarditis, a well-known complication of S.L.E., occurs in almost all patients at some stage of the disease. Of 7 patients without necropsy evidence of pericarditis, 5 died exceptionally and suggestively early in the course of the disease. Pericarditis usually appears as an isolated or a recurrent attack and is frequently painless; no fewer than 52 patients showed electrocardiographic abnormalities consistent with acute or chronic pericarditis at some stage of the disease.

During the disease 26 patients developed a diastolic blood pressure of over 95 mm. Hg, which was attributed to renal disease in 20 cases. Corticosteroid therapy had been given to 13 of these patients and occasionally aggravated the hypertension, but of the 6 patients with hypertension not due to renal disease, 4 had received steroid therapy. Congestive heart failure developed in 22 patients, systemic hypertension being the main, but rarely the sole, cause; other contributary causes were pericarditis, fever, secondary infection, anaemia, and sodium and water retention. The response of the heart failure in these patients to sodium restriction, digitalis,

and mersalyl was usually poor. In 2 cases an increase in the dosage of cortisone controlled the disease better and the heart failure improved, but generally the heart failure is made worse by administration of salt-retaining corticosteroids. *J. Warwick Buckler*

728. **Desoxyribonucleic Acid (DNA)–Bentonite Flocculation Test for Lupus Erythematosus**
J. Bozicevich, J. P. Nasou, and D. E. Kayhoe. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **103**, 636–640, March, 1960. 12 refs.

This paper from the National Institute of Allergy and Infectious Diseases, Bethesda, Maryland, describes another test for systemic lupus erythematosus (S.L.E.) depending on the affinity of L.E. serum for deoxyribonucleic acid (DNA). In this test, which is similar to the bentonite flocculation test for rheumatoid arthritis, bentonite particles are coated with DNA and bovine plasma albumin is added to prevent the particles from clumping. The addition of L.E. serum (not plasma) causes flocculation, but the reaction is more difficult to read than in the test for rheumatoid arthritis.

The DNA–bentonite flocculation reaction was positive in all of 8 cases of active S.L.E. (in all of which the result of the L.E.-cell test was positive) and in 2 out of 5 cases of S.L.E. in remission (with a positive L.E.-cell reaction in 4). The reaction was negative with 138 sera from patients without S.L.E., including 6 cases of rheumatoid arthritis with positive L.E.-cell reactions.

M. Wilkinson

729. **Ischemic Neuropathy in Necrotizing Arteritis**
G. W. Holt. *Neurology* [*Neurology (Minneap.)*] **10**, 43–50, Jan., 1960. 4 figs., 26 refs.

From the University of Colorado School of Medicine, Denver, the author describes one fatal case of periarteritis nodosa which followed cortisone therapy and a further case in which, however, the patient recovered on withdrawal of therapy; the lesions in the former case were confirmed histologically. In a review of the literature he has found 36 reported cases of arteritis occurring in cases of rheumatoid arthritis treated with steroids. The three cardinal symptoms are progressive neuropathy, widespread multiple involvement of the organs, and constitutional reaction.

The author's first case occurred in a female patient aged 51 with a history of rheumatoid arthritis for 3½ years, during which she had received 25 to 75 mg. of cortisone daily together with supplements of other steroids, gold, and salicylates. Burning and sensations of tingling developed in the hands, followed by wrist and foot drop. Progress was intermittent, but by the end of 6 months there was generalized paralysis and areflexia. Purpuric skin eruptions appeared, followed by gangrene, first of the rheumatic nodules in the hands and later involving the nail cuticle. The gangrene spread to include the finger tips and around the ankles. Patches of viable tissue in the midst of gangrenous areas suggested disseminated arterial lesions. At necropsy a necrotizing arteritis, indistinguishable from periarteritis nodosa, was found to be widespread in the viscera and particularly in the vasa nervorum of the vagus nerves. The second case was seen in a 39-year-old woman with rheumatoid arthritis who had been treated for over 5 years with corticosteroids. She suffered from weakness and hypoalgesia of the extremities and showed loss of reflexes, cyanosis, and impending gangrene of the fingers and toes. The cortisone was withdrawn under cover of a week's treatment with ACTH (corticotrophin). A week later the punctate gangrenous lesions and the peripheral cyanosis had disappeared, the neuropathy showed some improvement, and the rheumatoid nodules also cleared up. Observation for a year has revealed no return of these signs and symptoms.

The author discusses the mechanism of arteritis in such cases and comes to the conclusion that it is a sensitization phenomenon related to the tuberculin and Herxheimer reactions. *William Hughes*

730. **Lesions of the Heart in Systemic Scleroderma**
(Поражение сердца при системной склеродермии)
N. G. Guseva. *Терапевтический Архив* [*Ter. Arh.*] **32**, 30–38, Feb., 1960. 2 figs., 26 refs.

Cardiac involvement in scleroderma was first described in detail by Weiss *et al.* in 1943 (*Arch. intern. Med.*, **71**, 749), although a single case had earlier been reported by Heine in 1926 (*Virchows Arch. path. Anat.*, **262**, 251). In the present communication the author describes her investigations in 15 cases (including 4 at necropsy), all the patients having cardiac symptoms of varying degree, including dyspnoea, tachycardia, precordial pain, and arrhythmia (extrasystoles or gallop rhythm). Radiography revealed moderate enlargement of the heart to the left in 7 cases and unfolding of the aortic arch in 10; electrocardiographic changes present in 14 cases consisted in low voltage in 11, left axis deviation in 7, right axis deviation in 6, a widened QRS complex in 5, S–T displacement in 8, and abnormalities of the T wave in 13. Pathological examination of the heart muscle in the 4 fatal cases revealed myocardial involvement by the sclerodermal process. The coronary arteries were intact, but the smaller vessels showed fibrinoid infiltration and narrowing of the lumen, and the muscle fibres adjacent to the patches of cardiosclerosis were hypertrophied. All three layers of the heart were involved, and there was slight pericardial exudate. Mitral stenosis was present in all 4 cases, while there were lesions of the aortic valve in 2 cases and of the tricuspid valve in 3.

The condition is sometimes mistaken for rheumatism and in 5 of the author's cases this was the first diagnosis. Subjective symptoms are often absent in the early stages. Treatment is unsatisfactory, but the prolonged administration of steroid hormones is insisted upon.

L. Firman-Edwards

731. **Systemic Lupus Erythematosus: a Review of Certain Current Pathogenetic Concepts**
P. Altrocchi. *Journal of Chronic Diseases* [*J. chron. Dis.*] **11**, 34–49, Jan., 1960. 2 figs., bibliography.

Physical Medicine

732. **The Stretch Reflex in Man**
G. TARDIEU, P. RONDOT, J. C. DALLOZ, J. MENSCH, and C. MONFRAIX. *Cerebral Palsy Bulletin* [*Cerebral Palsy Bull.*] 14–17, No. 7, 1959. 5 refs.

The authors describe the results of experiments in which the electromyograph, the strain gauge, and the high-speed camera were used in an attempt to find a scientific method of measuring and classifying the various types of stiffness found in patients with cerebral palsy. The stretch reflex elicited by passive extension of the elbow at various speeds in a supine, relaxed patient were studied by these methods. Each type of stiffness, namely, rigidity, spasticity, and "tension" (the hypertonus of athetoid cerebral palsy) was found to produce a typical picture.

By electromyography a "limit speed" of extension could be defined for each case below which a flat record, that is, lower than 10 μv., could always be obtained in 60 testings in normal spastic and rigid cases. This "limit speed" was constant for each case and could be lowered by drugs. Tension athetoids on the other hand gave typically erratic results and no "limit speed" could be defined. The strain-gauge results in spastic and rigid cases were recorded graphically, the logarithm of the speed of extension being plotted against that of the force measured just before the end of passive movement, and a straight line was obtained. A formula, $F=KV^n$, was calculated, F being the force and V the speed; parameter K and exponent ^{n} define the degree of rigidity. The correlation of this formula was very high ($r=0{\cdot}9$ in rigidity and 0·89 in spasticity). Once again tension athetoids gave erratic results. High-speed camera records were also found useful in differentiating the different types of stiffness and in measuring results.

Janet Q. Ballantine

733. **Vascular Responses of Human Skin to Infra-red Radiation**
G. W. CROCKFORD and R. F. HELLON. *Journal of Physiology* [*J. Physiol. (Lond.)*] **149**, 424–432, Dec., 1959. 6 figs., 12 refs.

In this paper from the Medical Research Council Unit for Research on Climate and Working Efficiency, Oxford University, a study is reported of the effects of infrared radiation on the blood flow in the human forearm. A 75-watt lamp was used as the heat source at a distance of 22 cm. The blood flow in the forearm was measured by a strain-gauge plethysmograph and the blood flow in the hand by a water-filled plethysmograph. Subcutaneous temperatures were measured by thermocouples. In two experiments blood was taken from a deep vein in the forearm and analysed for oxygen content.

The results are plotted on a number of graphs. There was a rapid increase in total blood flow in the forearm during heating, with a slow return to the original level. No changes occurred in the opposite arm or in the hand on the same side as the heated forearm, but the whole of the forearm blood flow was increased, even if part was shielded from irradiation. The subcutaneous temperature rose approximately 4° C. There was no change in the oxygen content of blood taken from a deep vein, but blood from a superficial vein had an oxygen content similar to that of arterial blood during and after irradiation. Discussing the results and those of other workers the authors state that the vasodilatation is confined to the skin vessels and that a neural mechanism is responsible for this local reaction.

[These results differ from those of the abstracter (M.D. Thesis, 1959, University of London), which showed that muscle blood flow in the leg is increased by infrared radiation.] *J. B. Millard*

734. **Changes in the Physical Thermoregulation in Man during Acclimatization in the Far North.** (Сдвиги в области физической терморегуляции у людей при акклиматизации на Крайнем Севере)
I. S. KANDROR. *Гигиена и Санитария* [*Gig. i Sanit.*] **25**, 6–12, March, 1960. 5 figs., 16 refs.

In experiments carried out to determine the changes taking place in physical, as opposed to chemical, thermoregulation in man during acclimatization to Arctic conditions the vascular reactions to the application of cold to the forehead or to immersion of the limbs (protected by a polythene bag) in water at 0° C. were studied, the skin temperature being recorded by means of thermocouples. Tactile sensation and ability to perform fine movements were tested before and after cooling. The experiments were conducted on the Arctic coast during the winter in a room at a low, moderate, or high temperature on 300 subjects who were all natives of temperate zones of the Soviet Union and had had different periods of service in the Arctic regions.

The results showed that acclimatization is accompanied by a raised threshold of pain sensation, increased lability of the vascular reactions in the cooled area, inhibition of the vascular tone in the more distal parts of the limbs, and reflex reactions in the deeper tissues and the uncooled parts of the body. The last two of these may be concerned in the raising of resistance to the common cold and the first two in increasing the functional capacity of the organs concerned in work. These changes take place during the first year of acclimatization and are accompanied by a fall in the general morbidity rate. It is suggested that they should be taken into consideration when planning "hardening" and training programmes for persons who are to be subjected to severe cold, and also in the design of protective clothing.

Basil Haigh

Neurology and Neurosurgery

735. **Serial Electroencephalography in Brain Tumors and Cerebrovascular Accidents**
D. SILVERMAN. *A.M.A. Archives of Neurology* [*A.M.A. Arch. Neurol.*] **2**, 122–129, Feb., 1960. 8 figs., 15 refs.

Serial EEG's [electroencephalograms] were obtained on 42 patients with brain tumor and on 42 with cerebrovascular accidents. Although the long-established rule that tumors produce increasing focal EEG abnormality and cerebrovascular accidents produce diminishing abnormality was found to be generally valid, there were occasional exceptions with tumors and more frequent ones with cerebrovascular accidents. When close attention was paid to clinical details, dynamic electroencephalography provided a valuable contribution to our understanding of the underlying pathophysiology in brain tumors and cerebrovascular disease.—[Author's summary.]

736. **The Electromyographic Changes in Hyperkalaemic Familial Periodic Paralysis**
J. B. MORRISON. *Annals of Physical Medicine* [*Ann. phys. Med.*] **5**, 153–155, Feb., 1960. 5 figs., 6 refs.

The author reports the electrodiagnostic findings in 5 patients, members of the same family, suffering from the rare condition of hyperkalaemic familial periodic paralysis. The patients, 3 males and 2 females aged 7 to 54 years, were examined at Guy's Hospital, London. All had noticed previous episodes of weakness and were examined in both the active and quiescent phases. Before an attack of paresis electrical stimulation of the muscles was normal, but during an attack the response to faradism was reduced.

Electromyography gave the following findings. Before paresis: normal. During an attack: (*a*) fibrillation and spontaneous high frequency " dive-bomber " myotonic runs were noted; (*b*) on volition complex units of up to 7 to 8 phases with an amplitude of 250 to 300 μV. and a duration of 10 to 12 milliseconds were found; (*c*) also on volition were found high-frequency myopathic patterns of low amplitude lasting 2 milliseconds or less; (*d*) on attempted maximal volition the interference pattern was reduced.

The author states that the electromyographic changes are always typical during an attack and that this enables the condition to be differentiated from the more familiar hypokalaemic familial periodic paralysis.

Kenneth Tyler

737. **Reserpine in Huntington's Chorea**
W. H. KEMPINSKY, W. R. BONIFACE, P. P. MORGAN, and A. K. BUSCH. *Neurology* [*Neurology* (*Minneap.*)] **10**, 38–42, Jan., 1960. 25 refs.

The authors report from St. Louis City Hospital (Washington University School of Medicine), St. Louis, the therapeutic effects of reserpine in the treatment of Huntington's chorea in 10 patients aged 44 to 63. The drug was given orally in a dosage of 2 to 10 mg. daily together with 5 to 45 mg. of amphetamine sulphate given simultaneously to combat the asthenia induced by reserpine. The results were assessed by clinical observation and in more detail by the comparison of motion pictures taken before and during treatment.

All the patients showed a decrease in the severity of the choreic movements, there being in 2 complete cessation of these movements, in 6 a marked decrease, and in 2 a moderate decrease; 2 patients regained ability to walk while receiving the treatment. Unfortunately improvement only affected the physical pattern of symptoms and there was no corresponding change in the intellectual capacity. As a result, in one of the patients who regained the ability to walk reserpine had to be discontinued. Amphetamine counteracted the asthenic symptoms in some cases, but in one patient reserpine induced a state amounting to quadriplegia and this was not influenced by 10 mg. amphetamine daily; when reserpine was discontinued, however, this patient regained his former ability to walk. Hypotension after reserpine was corrected in one case by administration of ephedrine. In another case mild Parkinsonism developed. The authors discuss at length the nature of the abnormal movements in chorea. They observed that purposive voluntary movements blend imperceptibly with the abnormal movements and they regard chorea as a disorder of psychomotility.

William Hughes

738. **Dystrophia Myotonica: a Clinical and Electromyographic Study of the Effects of Certain Drugs on Myotonia**
N. PACHOMOV and J. E. CAUGHEY. *Neurology* [*Neurology* (*Minneap.*)] **10**, 28–37, Jan., 1960. 10 figs., 37 refs.

At Otago Medical School, Dunedin, New Zealand, the authors have studied both clinically and electromyographically the effects of various drugs upon the phenomenon of myotonia in 6 patients with " fully developed " dystrophia myotonica. The electromyogram (EMG) was recorded from the forearm muscles, using surface electrodes; the patient gripped an inflated sphygmomanometer cuff and then was given the command to relax, a recording being made every 5 minutes and the average duration of the myotonia then calculated.

Quinine sulphate in a dosage of 10 grains (0·65 g.) three times daily was given for 3 days and the EMG recorded 4 hours after the last dose; in 5 of the 6 patients the relaxation time was reduced. An EMG recorded one hour after the oral administration of 1 g. of procainamide showed that in 5 cases the relaxation time after this drug was greatly reduced, but in the 6th the improvement was less striking. Considerable reduction in myotonia also resulted from the administration of 100 mg. of

cortisone 12 hours before recording the EMG, while a similar but less striking effect was produced by 50 g. of glucose given orally followed by 0·1 unit of soluble insulin per kg. body weight given subcutaneously, but clinical improvement of the myotonia was negligible; no signs of hypoglycaemia were observed. A slight reduction in the myotonia was also produced by the administration of 15 g. of glutamic acid orally one hour before recording and by 20 ml. of M/6 sodium lactate given intravenously. The authors suggest that the phenomenon of myotonia may be the result of an increased permeability of the muscle cell membrane, with a consequent disturbance of the electrolyte equilibrium in the muscle, and cite the work of Williams *et al.* (*Lancet*, 1957, **2**, 464; *Abstr. Wld Med.*, 1958, **23**, 126), who showed that in dystrophic muscle the potassium content was significantly decreased and the sodium content correspondingly increased. *John N. Walton*

739. **The Carpal-tunnel Syndrome in Pregnancy**
M. WILKINSON. *Lancet* [*Lancet*] **1**, 453–454, Feb. 27, 1960. 13 refs.

The carpal-tunnel syndrome in pregnancy is discussed with reference to 14 cases in which symptoms developed, usually during the last 3 months. Signs of compression of one or more cervical nerve roots were present in addition in 7 of the cases. The author suggests that fluid retention is an important factor in the aetiology of the syndrome during pregnancy. The majority of the patients improved spontaneously after delivery. Only in one patient in whom symptoms persisted for several months was operation required.

J. W. Aldren Turner

740. **Hydrocortisone and the Carpal-tunnel Syndrome**
J. B. FOSTER. *Lancet* [*Lancet*] **1**, 454–456, Feb. 27, 1960. 12 refs.

The author of this paper from the Department of Medicine, King's College, University of Durham, describes the results obtained with hydrocortisone in the treatment of 20 patients with the carpal-tunnel syndrome, (unilateral in 15 and bilateral in 5). An injection of 1 ml. (25 mg.) of hydrocortisone tertiary butyl acetate was given into the carpal tunnel once a week for 3 weeks. Of the 25 carpal tunnels injected, there was complete relief of symptoms in 20 and some improvement in 3; there was no improvement in 2. In some patients relief of symptoms occurred after the first injection, but in others there appeared to be a delay of 3 to 8 months before the symptoms improved. The relapse rate, however, was high, symptoms recurring in 14 wrists 12 to 14 months after treatment. *J. W. Aldren Turner*

741. **A Clinical and Electrical Study of Ulnar Nerve Lesions in the Hand**
P. EBELING, R. W. GILLIATT, and P. K. THOMAS. *Journal of Neurology, Neurosurgery and Psychiatry* [*J. Neurol. Neurosurg. Psychiat.*] **23**, 1–9, Feb., 1960. 6 figs., 11 refs.

In this paper from the National Hospital, Queen Square, London, the authors discuss the clinical and electrical findings in 9 cases of lesions of the ulnar nerve in the hand. In 7 cases the hypothenar muscles were spared and there was no sensory impairment. Four of these patients recovered gradually without operation and a fifth, on whom an exploratory operation was performed with negative results, also recovered; it seemed likely that repeated minor trauma of occupational origin was the causative factor of the nerve lesion. In the other 2 cases of this group operation showed a local lesion compressing the nerve—a synovioma in the palm in one and thickening of the pisohamate ligament in the other. In the remaining 2 cases there was mild involvement of the hypothenar muscles and slight sensory impairment; one of these patients recovered spontaneously and in the other operation disclosed a ganglion compressing the main ulnar trunk.

Electrical studies were carried out on all the patients and demonstrated marked slowing of conduction in the segment of nerve distal to the wrist, while slighter changes were also found in the proximal parts of the affected nerves. *J. W. Aldren Turner*

BRAIN AND MENINGES

742. **Procaine–Oil–Wax Pallidotomy for Double Athetosis and Spastic States in Infantile Cerebral Palsy**
H. NARABAYASHI, H. SHIMAZU, Y. FUJITA, S. SHIKIBA, T. NAGAO, and M. NAGAHATA. *Neurology* [*Neurology* (*Minneap.*)] **10**, 61–69, Jan., 1960. 7 figs., 35 refs.

Experiences with procaine–oil–wax pallidotomy in 80 cases of unilateral or bilateral athetosis are reported, with electromyographic analysis before and after the operation. Notable clinical improvement was obtained in 62·5% and slight in 27·5% of the cases; improvement in everyday activity and voluntary movement occurred in various degrees. In electromyograms, stretch reflex discharges of the tonic type, which are thought to be the essential basis for athetotic movement, are reduced notably by the procedure. This suggests an explanation of choreoathetosis as a disorder of muscle tone and emphasizes the importance of the pallidum in regulating the level of muscle tone.—[Authors' summary.]

743. **A Clinical and Pathologic Study of Akinetic Mutism**
H. CRAVIOTO, J. SILBERMAN, and I. FEIGIN. *Neurology* [*Neurology* (*Minneap.*)] **10**, 10–21, Jan., 1960. 10 figs., 35 refs.

Akinetic mutism, a term coined by Cairns *et al.* (*Brain*, 1941, **64**, 273), is a disturbance of consciousness characterized by absolute mutism and complete immobility, except for the eyes. The authors describe in detail the clinical and pathological findings in 8 cases of this disorder seen at New York University–Bellevue Medical Center since 1953 in 7 males and one female patient aged from 54 to 70. All the patients were motionless and speechless, but their eyes continually moved in all directions and remained open for long periods. Painful stimuli sometimes produced a withdrawal reaction, or if the eyes were closed they would open in response to a sudden loud noise. Although

the patients seemed to be aware of their surroundings, there was no response to commands. All the patients died.

In 7 cases necropsy revealed partial or complete occlusion of the arteries of the vertebro-basilar system with multiple infarcts of the brain-stem, including portions of the reticular substance. In the 8th patient, a woman aged 57 who died after 81 days from carbon monoxide poisoning after exposure to coal-gas for 22 hours, there was extensive neuronal damage in the cerebral cortex and bilateral pallidal encephalomalacia. The authors conclude that akinetic mutism is usually the result of partial destruction of the reticular activating system in the brain-stem.

The mechanism by which the syndrome was produced in the case of coal-gas poisoning was not clear.

John N. Walton

744. **The Treatment of Disturbances of Consciousness in Neurosurgical Cases with the Dimethylaminoethyl Ester of *para*-Chlorophenoxyacetic Acid (ANP 235).** (Le traitement des troubles de la conscience en milieu neurochirurgical par l'ester diméthyl-amino-éthylique de l'acide *para*-chloro-phénoxy-acétique (ANP 235))
R. Coirault, H. Pourpre, R. Damasio, G. Rouif, P. Deligné, M. David, and J. Talarach. *Presse médicale [Presse méd.]* **68**, 215–216, Feb. 6, 1960. 3 refs.

From Val-de-Grâce and the Hôpital Sainte-Anne, Paris, the authors report the results of treating states of impaired consciousness with a new preparation, the dimethylaminoethyl ester of *p*-chlorophenoxyacetic acid (ANP 235). By mouth, the dose used was 0·4 to 1·2 g. in 24 hours, but doses as high as 4 g. have been given without producing toxic effects. Intravenously a slow injection of 1 ml. containing 250 mg. was given (in 30 seconds), and this could be repeated in an hour if necessary. Although the substance does not appear to have any toxic effects, even in high dosage, the authors consider its use to be contraindicated in inflammatory cerebral disease as it might cause an exacerbation of the infective process.

ANP 235 was found useful in treating coma following head injury. In one case of head injury complicated by anoxia the patient was still comatose and decerebrate 2 months after injury. Within 5 days of starting treatment with ANP 235 he was sufficiently conscious to follow a radio programme. Another patient, who had been stuporose for 3 months, made a gradual recovery in the month following treatment. One case of diabetes insipidus following head injury was controlled by treatment with ANP 235. Further examples are given of impaired consciousness following a posterior fossa operation, removal of the frontal lobes for metastatic tumour, hemispherectomy for glioma, and operations for medulloblastoma of the vermis and for craniopharyngioma. In all of these cases the level of consciousness improved following treatment and recovery was attributed to the drug.

The authors have also noted a favourable effect in confusional states following the surgical treatment of Parkinsonism.

Brodie Hughes

745. **Observations on 500 Cases of Migraine and Allied Vascular Headache**
G. Selby and J. W. Lance. *Journal of Neurology, Neurosurgery and Psychiatry [J. Neurol. Neurosurg. Psychiat.]* **23**, 23–32, Feb., 1960. 3 figs., 28 refs.

In this paper from the Northcott Neurological Centre, Sydney, the authors analyse the clinical features in 500 patients suffering from migraine. (The term is used to include paroxysmal generalized headaches in addition to unilateral ones.) They emphasize the fact that impairment of consciousness may at times occur with the headache and that this is more frequent when there are other symptoms of cerebral dysfunction. The pathogenesis of the migraine syndrome is discussed in relation to periodic autonomic instability and the selective susceptibility of individual cranial arteries.

J. W. Aldren Turner

746. **Effect of Serotonin in Migraine Patients**
R. W. Kimball, A. P. Friedman, and E. Vallejo. *Neurology [Neurology (Minneap.)]* **10**, 107–111, Feb., 1960. 5 figs., 12 refs.

The study here reported from the Montefiore Hospital, New York, was designed to determine whether serotonin (5HT), its precursor 5-hydroxytryptamine (5HTP), and monoamine oxidase inhibitors have any effect upon migrainous headache. It is known that reserpine, which releases endogenous 5HT, precipitates headache in migrainous subjects. Neither 5HT itself, however, nor its precursor caused headache when given intravenously to 35 such patients, even in very large doses. Both, on the other hand, abolished spontaneous migrainous headaches, and 5HTP also abolishes reserpine-induced headaches. Again, migrainous headaches were not induced by blocking monoamine oxidase by the administration of phenelzine in doses of 75 mg. daily for a week or by blocking the peripheral action of 5HT by the administration of 2-bromo-L.S.D. in doses of 1·25 mg. daily for a week. In fact both these compounds markedly reduced the frequency and severity of migrainous attacks.

The authors analyse these findings and suggest that the headache induced by reserpine is probably not the effect of the release of 5HT. The diverse and often multiple pharmacological effects, operating both peripherally and centrally, of these compounds do not allow the authors to draw any satisfactory conclusions from their results about the mechanism of migrainous headache.

J. B. Cavanagh

747. **Cerebral Angiography in the Diagnosis of the Acute Stroke**
J. W. D. Bull, J. Marshall, and D. A. Shaw. *Lancet [Lancet]* **1**, 562–565, March 12, 1960. 19 refs.

The value of angiography in the diagnosis of acute stroke was studied in 80 consecutive patients admitted to the National Hospital, Queen Square, London, and subjected to angiography within 72 hours of the onset of the acute attack. Of the 80 patients, 5 were in the 4th decade, 21 in the 5th, 38 in the 6th, and 16 in the 7th. The vascular territory supplied by one major vessel, either the common carotid or the vertebral artery, was examined. No abnormality was detected in 46 cases.

In 16 the findings on angiography agreed with the clinical diagnosis. Occlusion of the internal carotid artery was demonstrated in 14 cases, but had been diagnosed in only 4. Of 8 cases of occlusion of the middle cerebral artery, the clinical diagnosis was cerebral haemorrhage in 3 and occlusion of the internal carotid artery in 1. An increase in the severity of hemiparesis, hemianaesthesia, dysphasia, and hemianopia was observed in 9 cases after angiography, but these complications were transient. Angiography was helpful in 17 cases in revealing lesions which had not been diagnosed clinically. The authors emphasize, however, that this procedure is not justified in all patients with an acute stroke and that its place in the management of these cases cannot be finally assessed until the value of the various forms of treatment is known. *G. de M. Rudolf*

748. **Recurrent Cerebrovascular Episodes**
D. DENNY-BROWN. *A.M.A. Archives of Neurology* [*A.M.A. Arch. Neurol.*] **2**, 194–210, Feb., 1960. 5 figs., 39 refs.

The author of this paper from the Boston City Hospital and Harvard Medical School refers to the theory postulated originally by him in 1951 that transient hemiplegic episodes were due not to vasospasm, but to a state of carotid or basilar insufficiency determined by stenosis or occlusion of the artery and precipitated by a situation that lowered the systolic blood pressure or cardiac output. "On this basis, carotid or basilar insufficiency was a physiological, potential haemodynamic state, in which reversible *haemodynamic crises* could be elicited by any factor that impaired the collateral circulation." The symptoms are transient and completely or partially reversible depending on whether the crisis is so prolonged or so severe as to produce anatomical damage. The state of the intracranial collateral vessels is considered to be of prime importance in the production of the condition.

In the present paper the author examines some special features of carotid and basilar insufficiency and discusses the question of vasospasm. In the healthy monkey the occlusion of a vessel the size of the carotid artery does not produce symptoms unless the collateral circulation has been rendered insufficient by lowering the blood pressure by bleeding or drugs. Study of the arterioles in the experimental animal shows that when the blood pressure is lowered a further factor comes into play in the form of "venous microstasis" due to endothelial damage to the capillaries by anoxia, and that when this occurs infarction follows. The critical requirements for the avoidance of lesions are therefore: (1) an adequate level of systolic blood pressure or cardiac output; (2) sufficient fall in cerebrovascular resistance in the affected area to allow the collateral blood flow to develop before damage to the vascular endothelium and stasis occur, and (3) adequate oxygenation of the systemic arterial blood.

During induced cerebrovascular insufficiency in animals no arterial spasm is seen. Widespread spasm can, however, be induced by a sudden rise in intraluminal pressure. In hypertensive monkeys spasm of the arterioles has been observed, but this in itself gives rise to no insufficiency, though it does affect the anastomotic arterioles and comprises the collateral adjustment when occlusion of a major vessel occurs. There is little evidence that embolism causes widespread vascular spasm. In work with Meyer the author has observed and photographed a fibrin–platelet embolus lodging in a small peripheral branch of the middle cerebral artery. It broke up and passed into the capillaries without exciting spasm of the artery.

Attempts to find a test for cerebrovascular insufficiency are described. The obvious one of carotid compression was abandoned as being dangerous. Reducing the blood pressure by tilting, while it did not induce symptoms, did cause a characteristic slowing of the electroencephalogram (EEG) over the appropriate area in over 80% of cases. The most striking of such positive results were seen in elderly patients, and it was found difficult to induce EEG changes in younger patients by tilting. In the presence of hypertension, however, severe changes were readily induced. The author therefore concludes that there are factors associated with age and hypertension that impair collateral circulation and lead to a greater liability to hypotensive crisis. The existence of a minority of patients in whom neither an attack nor changes in the EEG can be induced by reduction of the blood pressure leads him to suspect strongly that there are two common types of cerebrovascular insufficiency.

Finally the author points out that adequate treatment should be directed towards counteracting the immediate cause of the haemodynamic crisis that gives rise to symptoms. In his experience this is more rewarding than anticoagulant therapy.

[This is an excellent paper and it is difficult to do justice to it in an abstract.] *N. S. Alcock*

749. **Neurosurgical Treatment of Spontaneous Intracranial Hemorrhage: Importance of Differential Diagnosis in "Cerebral Apoplexy" and Evaluation of Long-term Postoperative Results**
M. SCOTT. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **172**, 889–895, Feb. 27, 1960. 2 figs., 18 refs.

This paper from Temple University Medical Center, Philadelphia, presents a long-term follow-up report on 30 patients operated on for intracerebral bleeding. The sex distribution was equal and 75% of the patients were between 40 and 66 years of age, with extremes of 25 and 70. A table summarizing the clinical findings is given. Angiography was carried out in only 4 cases, in none of which was an aneurysm or vascular anomaly demonstrated. The indications for operation accepted by the author were symptoms and signs of increasing intracranial tension, signs of focal brain involvement, pineal shift, or angiographic evidence of vessel displacement or a vascular malformation. Operation was avoided in cases of capsular haemorrhage on the dominant side and in cases of advanced cardiovascular, renal, or pulmonary disease. The operative procedure consisted in a small craniotomy, removal of clot and inspection of the cavity wall, and sometimes biopsy of the wall. Rupture of an

artery without aneurysm was found in 3 cases, aneurysm in one, cerebral tumour in 2, and no cause for the bleeding in 24.

A capsular haemorrhage was found in 20 cases. Ten of these patients died in hospital and 6 died later after periods of 3 months to 6 years. The remaining 4 patients have survived for periods of 8, 9, 10, and 10 years respectively, giving an 8-year survival rate of 20%. All these patients were left with a severe neurological deficit and the 5 who were left totally hemiplegic all died within 2 years of operation. Clot within the temporal lobe was found in 7 patients. All survived operation, but 3 died later and one was not followed up, the remaining 3 having remained alive for periods of 7, 10, and 11 years respectively. These patients were left with less neurological deficit than those with capsular haemorrhage, the disabilities usually consisting in visual field loss and mild hemiparesis. Of 3 patients who had a subdural haematoma, one died and 2 were alive and well 11 years later. In the whole series the incidence of epilepsy was 32% among the 19 patients surviving operation. Necropsy was performed on 10 of the patients who died. Cerebral tumours were found in 2 and in the remainder the usual finding was persistent bleeding with cerebral softening. A further group of 8 cases with an operative mortality of 25% and short follow-up is reported briefly and a short analysis of the previous literature is given.

The author points out that the operative mortality in cases of haematoma of the temporal lobe is surprisingly small and that of 6 patients whose fate was known, 3 were alive 7 to 11 years after operation. On the other hand the operative mortality in cases of capsular haemorrhage is high and all the patients in his series with this lesion who survived operation had severe neurological deficit. Nevertheless, most of them would have died without operation, whereas 20% were alive 8 to 10 years after treatment and were leading useful lives.

Brodie Hughes

750. **Immediate Treatment of Cerebral Infarction: Seven Years' Personal Experience**

A. B. CARTER. *Lancet* [*Lancet*] **1**, 345–351, Feb. 13, 1960. 26 refs.

The author describes his experience at Ashford Hospital, Middlesex, in the early treatment of cerebral infarction by various different measures. In discussing definitions he prefers the term infarction to thrombosis, since in many cases it is not possible to demonstrate a clot in the brain post mortem to account for the lesion and he considers that stenosis of the internal carotid and cerebral arteries in the neck is a common cause of cerebral infarction distally. Of 1,002 cases clinically diagnosed as "stroke" during the period 1952–8 inclusive, 510 with cerebral infarction are considered in this paper; embolism was believed to be the cause in 85 of these cases. Up to 1956 mitral stenosis was the commonest cause of embolism, but since then cardiac infarction has become more common. The differential diagnosis between a stroke due to extracranial arterial stenosis, with or without thrombosis, and cerebral ischaemia without thrombosis is always difficult and often impossible. When anticoagulant therapy is being considered the important differential diagnosis is between infarction and intracranial haematoma due to circumscribed bleeding from any cause. In cases of non-embolic infarction reliance may be placed on such criteria as slow onset, step-wise course, a clear cerebrospinal fluid, and a normal blood pressure (to exclude bleeding).

In 1952 cerebral embolism was treated with repeated stellate ganglion block, with results no better than in an untreated series of patients admitted in 1953. Since 1954 anticoagulants have been used, with or without one stellate block; patients treated within a week of onset showed significant improvement. In the other forms of cerebral infarction stellate ganglion block in 1953 did not produce better results than in patients seen in 1952 to whom no specific treatment was given. The results improved in 1954 when carbon dioxide inhalation therapy was introduced and still further in 1955 with the addition of anticoagulants, this improvement being notably significant in cases of slow onset. In 1956 stellate ganglion block and CO_2 therapy were discontinued, and anticoagulant treatment alone has now been given a controlled trial in a selected group of 66 patients aged up to 70 years with a recent history of slow onset and with a diastolic blood pressure below 120 mm. Hg, alternate patients being given anticoagulant treatment. Therapy was begun with 12,500 units of heparin intravenously and continued with phenindione orally, 150 to 200 mg. daily, or sufficient to maintain the prothrombin time at between two and three times the normal; this treatment was usually given for up to 4 weeks. Of the 33 treated patients, 25 (75%) improved or recovered compared with only 18 (54%) of the 33 untreated, a just significant difference. The difference was significantly increased, however, if only those cases in which the lesion was adjudged "incomplete" at the start of therapy were compared—80 and 50% respectively. The author draws attention to the known dangers of anticoagulant therapy, but considers the results worth while in selected cases. Among absolute contraindications to their use he mentions the finding of blood and xanthochromia in the cerebrospinal fluid and severe hypertension. Special caution is necessary in patients aged over 70, in cases of sudden onset, and in those in which there is prolonged unconsciousness.

William Hughes

751. **Use of ^{82}Br in Differential Diagnosis of Lymphocytic Meningitis**

A. CROOK, H. DUNCAN, B. GUTTERIDGE, and C. PALLIS. *British Medical Journal* [*Brit. med. J.*] **1**, 704–706, March 5, 1960. 8 refs.

In healthy subjects a blood–cerebrospinal fluid (C.S.F.) barrier acts to maintain the ratio of the blood bromide level to the C.S.F. bromide level at about 2·6 to 2·9. It has been shown by various workers that in meningitis of varied aetiology this barrier becomes less effective and the ratio falls. In this study, carried out at the Postgraduate Medical School of London, the authors used the radioactive isotope of bromine (^{82}Br) to determine the bromine partition ratio between the serum and the C.S.F. in 7 patients with signs or symptoms of

meningeal irritation. An oral dose of 50 μc. of ^{82}Br as sodium bromide was given in 50 ml. of water. The first 5 ml. of C.S.F. obtained by lumbar puncture was taken for estimation, together with 5 ml. of blood. Equal volumes, usually 1 or 2 ml., of serum and C.S.F. were counted in a well-type scintillation counter, the ratio of these counts, corrected for background and " dead-time ", giving the bromide partition ratio. As a control this ratio was also determined in 30 patients without clinical evidence of meningitis and was found to range between 1·9 and 3·7, with a mean of 2·6.

Of the 7 patients with symptoms of meningitis the partition ratio in 5 was within the normal range and these were subsequently diagnosed as cases of non-tuberculous lymphocytic meningitis. In the remaining 2 patients, however, the partition ratio was grossly affected, the figure being 0·9 in both cases. Subsequently the diagnosis of tuberculous meningitis was confirmed by means of culture of the C.S.F. and guinea-pig inoculation. The authors thus conclude that the use of labelled bromide provides a simple test which enables a rapid differential diagnosis to be made in cases of lymphocytic meningitis of undetermined aetiology. *I. M. Rollo*

752. Results of Chemopallidectomy and Chemothalamectomy

T. H. LIN and I. S. COOPER. *A.M.A. Archives of Neurology* [*A.M.A. Arch. Neurol.*] **2**, 188–193, Feb., 1960. 1 fig., 5 refs.

This paper from St. Barnabas Hospital for Chronic Diseases and the New York University Post-Graduate Medical School reviews the effects of chemopallidectomy and chemothalamectomy on 100 patients aged 60 or over with a view to elucidating the indications for operation as well as its results. The ages of the patients varied from 60 to 71, with a mean of 63; 69 were men and 31 women; 96 of the group were right-handed and in 60 symptoms presented on the right. In 83 the upper limbs were first involved; tremor was the initial symptom in 64 and rigidity in 32, while both symptoms occurred together in 4. The duration of the illness ranged from one to 33 years with a mean of 7·3 years. Preoperative examination revealed tremor, rigidity, and bradykinesia; the vast majority of the patients showed impairment of skilled movements, one-third of them having difficulty in gross volitional activities such as walking. Other signs were masking of the face, dysarthria, dysphonia, hyperhidrosis, hypersalivation, and urinary retention. The patients were divided into three groups according to what was considered to be the chance of providing surgical relief: (1) good (42 patients), with predominantly unilateral involvement and carrying on a full-time occupation; (2) fair (42 patients), with more severe signs and requiring partial assistance in ordinary daily activities; and (3) poor (16 patients), with severe incapacity, autonomic disturbance, and mental abnormality.

The surgical treatment consisted in chemothalamectomy in 72 cases and chemopallidectomy in 45 cases, 13 patients being subjected to re-operation and 4 having bilateral operations. The mean duration of hospitalization was 28 days. Taking all groups together the results were excellent in 68%, the patient's condition was somewhat improved in 25%, and there was no improvement in 7%. The results were very much better in Group 1 than in Groups 2 and 3. Thus an excellent result was produced in 83% of Group 1, 65% of Group 2, and only 38% of Group 3. Age itself did not appear to affect the results, but chemothalamectomy produced an excellent result in 78% of cases, whereas chemopallidectomy achieved this in only 53%. Long-term follow-up (average 19·6 months) suggests that the initial good results have been maintained. In 35 cases the patient exhibited transient morbidity, the commonest forms being mental confusion (in 12·8% of the total), dysphasia (in 12·8%), and hemiparesis (in 5·1%). The operative mortality was 3%, death being due to haemorrhage in each case. *J. E. A. O'Connell*

753. Prolonged Behavioral Disturbances as Ictal Phenomena

E. S. GOLDENSOHN and A. P. GOLD. *Neurology* [*Neurology (Minneap.)*] **10**, 1–9, Jan., 1960. 5 figs., 35 refs.

From Columbia University and the Neurological Institute of the Presbyterian Hospital, New York, the authors describe the clinical and electroencephalographic (EEG) findings in 5 patients (2 adults and 3 children) all of whom had manifested episodes of altered behaviour and of emotional and intellectual disturbance lasting up to 72 hours, the attacks being typically of rapid onset and ending equally abruptly. The characteristic clinical features observed during these prolonged attacks included confusion, hostility, negativism, withdrawal, or a " dreamy state ", and these were often associated with motor activity manifested by myoclonic jerking, lip-smacking, and sometimes complicated, apparently purposeful, activity. Consciousness was never completely lost, but awareness was impaired and intellectual function was moderately depressed; however, all except one patient could recall accurately events occurring during the attacks.

The EEGs recorded during the episodes showed in all cases continuous or almost continuous, bilaterally synchronous, paroxysmal slow waves and spikes, sometimes irregular in outline and relationship, but often showing the spike-and-wave discharges at 2 to 3 c.p.s. characteristic of epilepsy. The authors point out that, apart from their duration the observed behavioural changes were indistinguishable on clinical grounds from those of temporal-lobe epilepsy, although in no case were the electrical abnormalities localized to the temporal lobe. They conclude that these cases demonstrate that prolonged abnormal behaviour may be the sole manifestation of an epileptic seizure and draw attention to the possibility that such an attack may readily be confused with a functional psychiatric disorder, such as psychosis or psychoneurosis. *John N. Walton*

754. The Beginnings of the National Hospital, Queen Square (1859–1860)

M. CRITCHLEY. *British Medical Journal* [*Brit. med. J.*] **1**, 1829–1837, June 18, 1960.

Psychiatry

755. **Distribution of Androgyny in Mental Patients**
J. H. REY and A. J. COPPEN. *British Medical Journal* [*Brit. med. J.*] **2**, 1445–1447, Dec. 26, 1959. 2 figs., 16 refs.

The discriminant androgyny score of Tanner was calculated for 53 male and 50 female control subjects, the latter being taken from among patients attending an antenatal clinic, and compared with the scores of 86 schizophrenic patients (40 male), 94 depressives (31 male), and 51 neurotics (22 male).

There were significant differences in the mean androgyny score and the mean biachromial diameter between the controls and each of the patient groups of the same sex, the scores of all the patient groups tending to be smaller. It is suggested that this is a result of a lack of development from the neutral type, which is basically feminine. This would account for the fact that the greater abnormality appeared in male patients. It has been reported that there is a significant correlation between androgyny and the size of the penis and between biachromial diameter and hirsuties and oligomenorrhoea in females. *D. J. West*

756. **The Axial Syndrome Common to all Psychoses.** (Das allen Psychosen gemeinsame Axialsyndrom)
B. LLOPIS. *Fortschritte der Neurologie, Psychiatrie und ihrer Grenzgebiete* [*Fortschr. Neurol. Psychiat.*] **28**, 106–129, Feb., 1960. 40 refs.

The malnutrition prevalent in Madrid during the Spanish Civil War gave rise to a large number of cases of pellagra. This provided the opportunity to follow cases through from the early stages to the end. The findings are of great general psychiatric significance and seem to lend support to the old concept of the " unitary psychosis ". The cases of pellagra had the following features: (1) Symptomatically, they showed not only " exogenous reactions ", but also pictures like those of the " endogenous " psychoses. (2) The various states did not appear at random, but seemed to appear in a definite order: first neurasthenic states, then thymopathic states, later schizophrenic states, then twilight states, and finally states of torpor. This shows that all these states are non-specific and their progression may be regarded as forming a parallel to the progression of transitory states of changing consciousness from the waking state to deep sleep. (3) Whereas those features of the syndrome concerned with changes in consciousness depended on the severity of the condition of the whole brain, the localized cerebral effects of the pellagra lesions determined the content of the syndrome—such symptoms as tingling, hyperhidrosis, burning sensations in the limbs, scotomata, tinnitus, and disturbances of deep sensitivity. In practice in every case the two types of syndrome occurred together, forming new syndromes.

The theoretical implications of these findings lead the author to support the concept, in a modified form, of the unitary psychosis as proposed by Griesinger. This concept saw the various syndromes merely as expressions of different stages of the same process. This view was pushed into the background by the work of Kraepelin, but has received renewed attention from such workers as Ey, Conrad, and others. *J. Hoenig*

757. **Reproducibility of the Mecholyl Test**
A. G. BLUMBERG. *Psychosomatic Medicine* [*Psychosom. Med.*] **22**, 32–41, Jan.–Feb., 1960. 22 refs.

At Hillside Hospital, Glen Oaks, New York, a reappraisal was made of the clinical value of the " mecholyl " (methacholine) test of Funkenstein in view of the recent controversy concerning its worth as a measure of responsivity to electric convulsion therapy (E.C.T.). In particular, its reproducibility was investigated. This type of validation was held to be of basic significance in determining the reliability of the test for the differentiation of clinical phenomena. Tests were conducted on 5 successive days upon 35 psychiatric patients (14 male, 21 female) aged 16 to 59. Blood-pressure recordings were made by a trained observer using the standard method on one arm and by means of an automatic recording sphygmomanometer on the other. Readings were made at one-minute intervals for 20 minutes.

The test was found to be reproducible to a reasonable degree when the basis of its interpretation was limited to the area enclosed by the systolic blood-pressure curve, but not when the methods of classification of Funkenstein (based on the shape of the blood-pressure curve) and of Gellhorn (based on the areas enclosed by the curve above and below an arbitrary base line) were employed. The use of the automatic recording sphygmomenometer was shown to improve the reliability of the test. It was calculated, furthermore, that on the basis of area computation the results of 2 consecutive tests are as useful clinically as those of 5. An additional calculation revealed that a correction for the basal blood pressure increased the reliability of the test. It is suggested that the large number of experimental variables may explain the failure of previous investigators to confirm the reproducibility of the test. *A. Balfour Sclare*

758. **Psychodynamic and Psychophysiological Aspects of Pseudocyesis**
D. C. GREAVES, P. E. GREEN, and L. J. WEST. *Psychosomatic Medicine* [*Psychosom. Med.*] **22**, 24–31, Jan.–Feb., 1960. 19 refs.

A report of an unusually interesting case of pseudocyesis is presented from the Medical Centers of the Universities of Kansas and Oklahoma. Both psychological and endocrinological aspects are discussed and detailed clinical data are supplied.

A woman of 37, married for the second time, was admitted to hospital with symptoms suggesting 4 months' pregnancy. The psychological background was one of insecurity since childhood, and she had always regarded sex with embarrassment and disgust. She was discovered to be suffering from diabetes mellitus at the age of 13. She had previously had one pregnancy during each of her marriages. On account of pre-eclampsia the second pregnancy culminated in foetal death, and hysterectomy was therefore performed subsequently. On examination it emerged that the patient, while professing a conviction that she was pregnant for a third time, knew that this was impossible anatomically. There was a strong desire to conceive again, for she had felt " only half a woman " since the hysterectomy. Her insulin requirement was diminished during the pseudocyesis, as it was during her two true pregnancies, but increased again after she had had a " false labour ". Although many of the physical signs of pregnancy were present during the pseudocyesis, the urinary gonadotrophin (FSH) assay was normal.

The syndrome was comprehensible in the light of the desire to be pregnant. Furthermore, it afforded a number of secondary gains; it served to deflect her husband's attention from another woman, thereby helping to cement the marriage and, incidentally, frustrating her mother's wish that it should fail. *A. Balfour Sclare*

759. **A Clinical–EEG Study in a Case of Obsessional Neurosis**

J. G. GIBSON and W. A. KENNEDY. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] **12**, 198–201, Feb., 1960. 1 fig., 13 refs.

The authors describe the clinical and electroencephalographic (EEG) findings in a 34-year-old female who was admitted to the Maudsley Hospital, London, suffering from an acute and disabling exacerbation of a lifelong obsessional disorder. For some 15 months before admission she had experienced a compulsive urge to act like a dog (growling and barking) and had also had fears that she would harm her mother by splitting her head with an axe. The first EEG, taken shortly after admission, showed frequent paroxysmal discharges of slow waves and spikes occurring over both hemispheres with variable asymmetry (there was no past history of epileptic seizures in the patient or her family). EEGs were then recorded weekly over a period of 5½ months, during which serum electrolyte values, urinary excretion of steroids, and carbohydrate metabolism were also studied. It was found that the incidence and severity of the paroxysmal spike-and-wave discharges showed a direct relationship with periods when the patient received a high-carbohydrate diet and with exacerbations of her mental state. On two occasions administration of potassium chloride appeared to have a deleterious effect both upon the EEG and upon the patient's symptoms. After a further 4 months when the patient was generally cooperative and placid attempts to provoke changes in the EEG with a high carbohydrate intake and potassium chloride failed and no paroxysmal discharges were seen. *John N. Walton*

760. **Delinquency Rates and Personality**

S. R. HATHAWAY, E. D. MONACHESI, and L. A. YOUNG. *Journal of Criminal Law, Criminology and Police Science* [*J. crim. Law*] **50**, 433–440, Jan.–Feb., 1960.

This paper from the University of Minnesota reports the results of further follow-up studies of children who were tested by the Minnesota Multiphasic Personality Inventory (M.M.P.I.) 3 years before. Previous work showed that boys scoring high on the psychopathic, schizophrenia, and hypomania scales of the test tended towards higher than average delinquency rates. Conversely, those scoring high on social introversion, depression, and masculinity–femininity tended towards less than average delinquency rates. On the basis of these findings two sets of test profiles were defined which were named " delinquency excitatory " and " delinquency inhibitory ". The other four scales of the M.M.P.I. showed no consistent association with delinquency.

In the present study 11,329 school-children in the ninth grade were tested by the M.M.P.I. Their average age was 14 and they were believed to constitute a representative sample of the population of Minnesota State. Among the boys, approximately a quarter had excitatory and another quarter inhibitory profiles. When police and court records were searched in the follow-up 3 years later it was found that the delinquency rate of those with the delinquency excitatory profiles was 20% higher than the average for the whole group, whereas that of the boys with delinquency inhibitory profiles was 20% lower than the average. The corresponding differentiation among the girls was still more marked, the rate for those with excitatory profiles being double the general delinquency rate and that for those with inhibitory profiles being 40% less than the general rate.

The results show that M.M.P.I. profiles derived from adult behaviour disorders are moderately associated with delinquent trends. Although the profiles are relatively weak predictors, they provide information for research. They suggest that both low and high delinquency rates may sometimes be symptoms of personality disturbance. Among the items on the M.M.P.I. questionary is one concerning previous trouble with the law. In the group with variable profiles more boys admitted to this than actually had police records, whereas only 80% of those in the excitatory group with such records answered the item positively. The authors give this as an example of the complexity of the responses, which cannot be summed up as simple error or lying but cannot easily be interpreted. *D. J. West*

761. **The Prediction of Delinquency from Non-delinquent Behaviour**

D. H. STOTT. *British Journal of Delinquency* [*Brit. J. Delinq.*] **10**, 195–210, Jan., 1960. 3 figs., 14 refs.

In attempts made in the past to develop a technique for predicting delinquency psychosocial tests have been applied to selected populations containing an artificially high proportion of delinquents. Walters (*Brit. J. Delinq.*, 1955, **6**, 297) made a calculation to show that the differentiating value of the predictive data of Glueck would be reduced from 89·2% to 14·13% if applied to a

normal population. Tests with a greater predictive range which will detect the less extreme cases are necessary.

The subjects of the study reported herein were 415 Glasgow boys aged 8 to 15 who were put on probation in 1957; they were matched against 404 non-delinquent boys from the same schools with, as nearly as possible, the same birth dates. All the boys were rated by their teachers on the Bristol Social Adjustment Scale, which aims to rate " stability " or " disturbance " on the basis of items of objectively observable behaviour. Only 23% of the delinquents, compared with 71% of the controls, came within the " normal boy " range, and 46% of the delinquents, compared with only 8% of the controls, fell into the " maladjusted " range. The differentiation was substantially increased by reducing the test to 54 adverse items, each of which was at least four times as frequent among the boys on probation as among the non-delinquent boys.

The items of greatest predictive value included those indicative of hostility to other children (from jealous rivalry to enmity and lack of human feeling), hostility to adults, unconcern for adult approval, truancy, and unpunctuality. It is stated that there is other evidence to suggest that disturbance of social behaviour precedes the onset of overt delinquency; the validity of these tests as predictors depends upon this assumption.

D. J. West

MENTAL DEFICIENCY

762. **Convulsions in Mentally Retarded Children With or Without Cerebral Palsy: Their Frequency and Age Incidence**

R. S. ILLINGWORTH. *Journal of Mental Deficiency Research* [*J. ment. Defic. Res.*] 3, 88–93, Dec., 1959 [received March, 1960]. 7 refs.

The author reports from the University and Children's Hospital, Sheffield, that among 285 mentally retarded children with cerebral palsy (Group 1) the incidence of convulsions was 37·5%, while among 444 without cerebral palsy (Group 2) it was 31·3%; no fits occurred among the 87 mongol children in the series and these were excluded from the analysis. In Group 1 the slightly to moderately retarded patients showed an incidence of 22·8% compared with 16·3% in Group 2. The corresponding figures among the severely retarded children were 53·7 and 46·8% respectively.

Consideration of the effect of prematurity showed that among the prematurely born with cerebral palsy the incidence of fits in slightly retarded children was 20·4% and in those without cerebral palsy 25·5%, but in the severely retarded the incidences were 53·6 and 27·2% respectively. Among the full-term slightly retarded the percentages were 26·8 and 13·7, and among the full-term severely retarded they were 53·6 and 51·6. Both in those with and those without cerebral palsy more than half had the first fit before the first birthday. In 14·8% of the cerebral palsy patients and in 9·7% of those without cerebral palsy the first fit occurred at school age.

G. de M. Rudolf

763. **The Neutral 17-Ketosteroid and 17-Ketogenic Steroid Excretion of Mongol and Non-mongol Mentally Defective Boys**

G. DUTTON. *Journal of Mental Deficiency Research* [*J. ment. Defic. Res.*] 3, 103–107, Dec., 1959 [received March, 1960]. 13 refs.

It has been shown that the skeletal development of mongols is normal in spite of the retardation of linear growth. Since steroids are closely related to protein metabolism and thereby to growth the author has investigated, at St. Lawrence's Hospital, Caterham, Surrey, the steroid excretion in 24-hour collections of urine from 33 mongol boys aged from 7 to 16 years, and as a control in similar specimens from 48 non-mongoloid mentally defective boys of the same age group. No preservatives were used and the analyses were begun within 3 hours of the ending of the collection. Creatinine was estimated by the alkaline picrate method and 17-ketosteroids by the modified method of Callow *et al.* and Robbie *et al.*, with the colour correction of Talbot *et al.*; 17-ketogenic steroids were estimated by a modification of the sodium bismuthate method of Norymberski.

The rise in daily urinary excretion of both keto and ketogenic steroids with the onset of puberty appears to occur at the same time and to a similar degree in mongols as in non-mongols. No significant differences in the levels of excretion of 17-keto and 17-ketogenic steroids in the mongols or controls were found. It is concluded that neither the level of function of the adrenal glands nor that of the gonads can be cited as the cause of failure in linear growth in mongols.

G. de M. Rudolf

764. **Endocrinological Aspects of Mental Deficiency. I. Testicular Function in Mongolism**

A. T. RUNDLE, G. DUTTON, and J. GIBSON. *Journal of Mental Deficiency Research* [*J. ment. Defic. Res.*] 3, 108–115, Dec., 1959 [received March, 1960]. 4 figs., 12 refs.

In this study of testicular function in mongolism, reported from St. Lawrence's Hospital, Caterham, Surrey, the urinary 17-ketosteroid excretion was investigated in 82 male and, for comparison, in 48 female mongols aged from 15 to 51 years, 24-hour specimens of urine being used. A control group consisted of 40 non-mongoloid mental defectives of the same ages.

Both groups of males underwent similar changes in the excretion level of 17-ketosteroids, this showing a spurt at puberty and reaching a maximum at age 23. The female mongols showed a much smaller pubertal spurt, and a slight increase in excretion level which reached a maximum at age 24. The rate of development of the two male groups towards steroid maturity was similar.

The six main steroid fractions were grouped together into the β group (Fractions I to III), probably all derived from the adrenal cortex, and the α group (Fractions IV and V), derived partially from testosterone and partially from dehydro-epiandrosterone, and Fraction VI, the II-oxo steroids, which are metabolites of the adrenal corticosteroids. No significant difference was found in the excretion of any of these steroid groups between 11 male controls and 12 male mongols all over

23 years of age. These results indicate that some degree of testicular function exists in mongols at least in so far as the testes, acting as endocrine glands, provide a source of androgens. *G. de M. Rudolf*

ORGANIC DISORDERS

765. **Symptomatic Psychoses (1941–1957).** (Symptomatische Psychosen (1941–1957))
U. FLECK. *Fortschritte der Neurologie, Psychiatrie und ihrer Grenzgebiete* [*Fortschr. Neurol. Psychiat.*] **28**, 1–72, Jan., 1960. Bibliography.

This review of symptomatic psychoses is based on a survey of the literature published between 1941 and 1957. [It is distinguished by its critical attitude and comprehensive inclusion of the literature of various countries. Besides the German literature, French publications are taken account of, and also the much smaller number of papers from Great Britain and America. As in most German surveys a great deal of attention is paid to questions of definition, philosophical foundation, and other general problems.] The paper is divided into two parts. The first is devoted to a general discussion of symptomatic psychoses and the second to the psychoses associated with various special conditions. Psychoses in infectious and rheumatic diseases and in illnesses connected with gestation and childbirth are dealt with, followed by psychoses associated with endocrine abnormalities, tumours of the brain, and cerebral operations. Post-traumatic psychoses are fully discussed, as are symptomatic psychoses in various neurological diseases and finally psychoses connected with malnutrition and metabolic disturbances. The author concludes with a quotation from Kretschmer: "One should not cut oneself off from insight into the real processes of life through too strict definitions; these processes are by nature neither logical nor systematic, but only living".

[A review of this type cannot be abstracted and must be read in the original.] *W. Mayer-Gross*

766. **Neurological and Psychopathological Syndromes in Subacute Bacterial Endocarditis and Their Importance for Early Diagnosis.** (Neurologische und psychopathologische Syndrome bei Endocarditis lenta und ihre Bedeutung für die Frühdiagnose)
A. GUNTERMANN. *Fortschritte der Neurologie, Psychiatrie und ihrer Grenzgebiete* [*Fortschr. Neurol. Psychiat.*] **28**, 77–106, Feb., 1960. Bibliography.

It is advisable to search for subacute bacterial endocarditis if a patient of any age suddenly develops a paranoid psychosis or transient confusion, aphasia, or hemiplegia. The commonest cerebral lesions in subacute bacterial endocarditis are embolism, with softening, and mycotic aneurysms; further, meningitis, encephalo-meningitis, and metastatic localized encephalitis may occur. Involvement of the central nervous system seems to occur in about one in every 4 cases. Of 142 cases of cerebral embolism seen at the University Nervous Clinic, Cologne, the diagnosis of endocarditis was made in 38 (23 female). Of these, 14 patients showed predominantly neurological symptoms and 6 psychotic pictures. The mental changes show the usual characteristics of the organic syndromes, from the mildest to the severest. There is often, in addition, very severe excitement. The diagnosis is often elusive. The following picture should arouse suspicion of endocarditis—the characteristic history, the non-specific findings (in particular the erythrocyte sedimentation rate), the cardiac changes, often very slight, with many neurological signs, changes in the cerebrospinal fluid, focal electroencephalographic abnormalities, epileptic seizures, and mental changes. *J. Hoenig*

767. **Use of Iproniazid in Treatment of Alcoholics**
J. C. TRAVIS. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **172**, 909–912, Feb. 27, 1960. 7 refs.

In this report from the Adult Guidance Centre, San Francisco Department of Health, the author first draws attention to the frequency of severe depression in alcoholics after drinking bouts, the patient's feelings of remorse, guilt, and hopelessness frequently leading him to contemplate suicide. Considering the risk of suicide to be greater than that of hepatotoxic effects, the author treated 10 men and 10 women suffering from such depression with the anti-depressant drug iproniazid. The ages of patients ranged from 35 to 67 years, the mean being 42 years. The initial psychiatric diagnosis varied, but severe depression was a common factor in all cases. Iproniazid was given by mouth, the dosage ranging from 25 to 150 mg. a day, for one to 40 (mean 9·8) weeks. Ancillary treatment consisted in the administration of "polyvalent vitamins", including pyridoxine (to minimize the possibility of peripheral neuritis due to iproniazid), constant supervision by means of frequent visits to the clinic, and psychotherapy in the nature of reassurance and consolation.

The results were classified as excellent (reversal of all symptoms) in 6 cases (4 women, 2 men), good (reversal of most symptoms and amelioration of others) in 6 (2 women, 4 men), fair (some amelioration of symptoms) in 4 (1 woman, 3 men), and poor in 4 (3 women, 1 man). A response, when obtained, was observed within a few days of starting treatment. The author states that the drug also helped the patients to refrain from alcohol. No side-effects of therapy were observed. No hospitalization was needed and no suicides occurred.

[Owing to the absence of controls and of statistical treatment, the concomitant ancillary treatment, and the smallness of the scale the work remains inconclusive. The results are encouraging, but need further experimental examination.] *N. Rathod*

768. **Brain Damage from Chronic Alcoholism: the Diagnosis of Intermediate Stage of Alcoholic Brain Disease**
A. E. BENNETT, G. L. MOWERY, and J. T. FORT. *American Journal of Psychiatry* [*Amer. J. Psychiat.*] **116**, 705–711, Feb., 1960. 12 refs.

The authors of this paper from Herrick Memorial Hospital and the Bennett Neuropsychiatric Research Foundation, Berkeley, California, set out to define and

describe a syndrome intermediate between acute reversible alcoholic brain disease (delirium tremens and acute intoxication) and the chronic irreversible stage (dementia, Korsakoff's psychosis, and Wernicke's encephalopathy). Of 227 cases of alcoholism studied, the condition was in the acute stage in 98, the chronic stage in 48, and the intermediate stage in 81. Clinical examination, psychological tests, and electroencephalography (EEG) were carried out on all patients in the intermediate stage. In 64 of them the EEG tracing was abnormal, but usually returned slowly to normal. The authors state that the patient in this stage is usually an addict, and a significant clinical sign is the appearance of temporary periods of amnesia about happenings during the drinking episodes. He becomes increasingly dependent upon alcohol and gives away to " alcoholic thinking " (intricate rationalizations, excuses, and lies). Emotional lability, hostility, poor judgment, and lack of insight complete the clinical picture. It is maintained that these symptoms are caused by the chronic toxic effects of alcohol and are " organic symptoms of brain damage ". Air encephalography in 4 of these patients revealed evidence of cerebral atrophy in 3.

The authors consider that vigorous treatment, from all aspects, can influence the course of the illness and prevent the development of the chronic stage of alcoholism. [No evidence is given in support of this view.]

B. M. Davies

SCHIZOPHRENIA

769. **Placebo Response in Schizophrenic Outpatients**

L. D. HANKOFF, D. M. ENGELHARDT, and N. FREEDMAN. *A.M.A. Archives of General Psychiatry* [*A.M.A. Arch. gen. Psychiat.*] **2**, 33–42, Jan., 1960. 18 refs.

The authors have investigated the implications of the response to placebo therapy in 103 schizophrenic outpatients who were so treated during the first 3 weeks of their attendance at the State University of New York Downstate Medical Center, Brooklyn. Of these patients, 50 had been previously admitted to a mental hospital for 2 to 3 weeks' observation and were seen within a week of their discharge; the other 53 were referred as outpatients for examination. Most of them came from lower socio-economic classes. Criteria for selection included an age range of 18 to 42 years and evidence of schizophrenic symptoms (but not necessarily of frank psychosis) for at least one year. A positive placebo response was defined as any symptomatic change attributed by the patient to the medication and was assessed on information contained in the progress notes.

A positive or favourable response was seen in 42 patients, no response in 41, and a negative or unfavourable response in 20. Absence of a positive response was significantly associated with failure of treatment, that is, failure to continue treatment or admission to a mental hospital within one week to one year of treatment. For recently hospitalized patients (only), a positive response predicted continuation in treatment of those who tended to deny their illness. From these and similar earlier findings the authors develop the concept of the placebo response as a non-verbal communication whose meaning arises in the treatment of a particular type of patient, in a given setting, during a specified phase of the treatment process. The present study has implications only for the treatment of poorly educated, inarticulate schizophrenics. They suggest that the significance of the placebo response in other situations requires re-definition of the patient population, the treatment relationships, and the setting.

Alan A. Black

770. **High Dosage Chlorpromazine Therapy in Acute and Chronic Schizophrenia**

R. H. V. OLLENDORFF. *American Journal of Psychiatry* [*Amer. J. Psychiat.*] **116**, 729–736, Feb., 1960. 7 refs.

Intensive chlorpromazine therapy in schizophrenia was tried on a group of 143 patients at Hellingly Hospital, Hailsham, Sussex. The dosage of the drug was gradually increased to a peak of 2,100 mg. daily, this peak dosage being continued for a week between the 12th and 19th days of treatment. Thereafter the dosage was reduced to a maintenance level of 300 to 600 mg. daily, which was given for an indefinite period. Modified electric convulsion therapy (E.C.T.) was given on three occasions during the build-up of the chlorpromazine dosage and on three occasions during reduction of the dosage. Side-effects were common and included drowsiness, orthostatic hypotension, epileptic manifestations, severe Parkinsonism, confusional states, and skin reactions. None of these was considered dangerous or called for cessation of treatment; jaundice did not develop in any of the patients during the treatment.

The author considers that this intensive treatment is a useful method of forcing a remission in schizophrenia. The results obtained in patients admitted for a first acute episode of schizophrenia, for a breakdown after a remission, and also in chronic schizophrenics in hospital are separately assessed; 35% of patients in the last group were able to be discharged from hospital after treatment. It is interesting to note that during the trial E.C.T. was given on 900 occasions to patients receiving an average of 900 mg. of chlorpromazine a day, and in no case was there any difficulty in the recovery.

B. M. Davies

771. **Drug Therapy in Schizophrenia: a Controlled Study of the Relative Effectiveness of Chlorpromazine, Promazine, Phenobarbital, and Placebo**

J. F. CASEY, I. F. BENNETT, C. J. LINDLEY, L. E. HOLLISTER, M. H. GORDON, and N. N. SPRINGER. *A.M.A. Archives of General Psychiatry* [*A.M.A. Arch. gen. Psychiat.*] **2**, 210–220, Feb., 1960. 5 figs., 21 refs.

This cooperative study was begun on 805 male schizophrenic patients all under the age of 51 years, 37 psychiatric hospitals under the Veterans Administration taking part. Of this initial number, only 692 completed the first half of the trial. The patients were classified in four categories consisting respectively of acute disturbed (7%), acute non-disturbed (12%), chronic disturbed (20%), and chronic non-disturbed (61%). The chronic patients had not received tranquillizing drugs for at least 2 months and the acute patients for at least one month. Patients in each of the four categories were then ran-

domly allotted to one of four treatment schedules: (1) chlorpromazine up to 400 mg. daily; (2) promazine up to 400 mg. daily; (3) phenobarbitone up to 200 mg. daily; and (4) a placebo (lactose), the drugs and the placebo being given by mouth in fixed, gradually increasing amounts in 2 or 3 doses daily for an initial period of 12 weeks. Neither the patients nor their physicians knew the nature of the medication. Side-effects did not help to distinguish the drugs since the most frequent side-effect produced by all three was drowsiness. The number of patients failing to complete the experiment was not significantly different in the four treatment groups. After the first 12 weeks the experiment was continued in 26 of the hospitals for a further 12 weeks (528 patients, three-quarters of them chronic non-disturbed cases, of whom 489 completed the course), during which each treatment group was divided into three parts, one continuing with the same medication, one with a tranquillizing drug and placebo, and one with phenobarbitone and placebo. The results were evaluated by two rating devices: (1) the multidimensional scale for rating psychiatric patients of Lorr *et al.*, the validity and reliability of which has been established, and (2) a global and intuitive estimate of psychiatric status.

It was concluded that, at least in chronic non-disturbed patients, chlorpromazine was more effective therapeutically than promazine and the latter more effective than either phenobarbitone or the placebo. Placebo medication, however, was superior to all three drugs in reducing self-depreciation. This result, it is suggested, may have been due to the tendency of the other drugs to aggravate depressive symptoms in some patients. Patients given the placebo also lost the symptom of resistiveness more often than those receiving phenobarbitone. *F. K. Taylor*

772. **Urinary Aromatic Excretion Patterns in Schizophrenia**

H. GOLDENBERG, V. FISHMAN, J. WHITTIER, and W. BRINITZER. *A.M.A. Archives of General Psychiatry* [*A.M.A. Arch. gen. Psychiat.*] **2**, 221–230, Feb., 1960. 4 figs., 26 refs.

The authors criticize previous chromatographic investigations which demonstrated increased aromaturia in schizophrenic patients on the grounds that they neglected to take into account differences in dietary habits, medication, and fluid intake, and because they relied on a mere visual scanning of chromatograms. In the present study, carried out at Hillside Hospital and Creedmoor State Hospital, New York, they tried to avoid these errors by (1) determining dietary influences on aromaturia; (2) screening all samples of urine for the presence of salicylates and phenothiazine-derived tranquillizing drugs; (3) correcting values for urine dilution by referring them to the urine creatinine content; and (4) assessing chromatograms objectively by a recording densitometer. In all, 134 schizophrenic patients and 129 normal subjects were investigated. At least two morning specimens of urine were collected from each subject and the analysis carried out in duplicate. All urines containing salicylates were excluded from the study; in no instance was phenothiazine detected. All chromatographic ratings were judged against an arbitrary standard of " artificial urine " examined simultaneously.

It was found that coffee, acetylsalicylic acid, prunes, pyridoxine, and to a less extent bananas influenced aromaturia. Tea and nicotinamide were variable in their effects. In normal subjects the excretion of aromatic substances and indican was found to be greatest in young children, decreasing in young adulthood, and rising again slightly in older age. Females tended to have higher values during puberty and middle age. These variations may have been partly due to the dependence of urine creatinine excretion on sex and age. In the schizophrenic patients the values of aromaturia and indican excretion were not significantly different from those in normal subjects. *F. K. Taylor*

TREATMENT

773. **The Effect of Meprobamate on the Electroencephalogram, during Treatment, Intoxication and after Abrupt Withdrawal**

N. BOKONJIC and W. TROJABORG. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] **12**, 177–184, Feb., 1960. 5 figs., 27 refs.

A study of the effects of meprobamate upon the electroencephalogram (EEG) of 66 patients (30 female and 36 male) without symptoms or signs of organic brain disease or epilepsy is reported in this paper from the University Hospital and the Institute of Neurophysiology, University of Copenhagen. The patients were divided into 3 groups: (1) 27 patients who received 5 to 25 mg. of meprobamate per kg. body weight 4 times a day; (2) 32 patients given a single therapeutic dose of 5 to 23 mg. per kg.; and (3) 7 patients who had taken 120 to 400 mg. per kg. in a suicidal attempt. Several recordings were taken over a period up to 6 weeks in 8 patients from Group 1, while 18 patients, also from this group, were examined during and after abrupt withdrawal of the drug.

It was found that with an intake of more than 30 mg. per kg. the EEG showed increased fast activity at 18 to 28 cycles per second, particularly in the parietal regions, while with an intake of more than 64 mg. per kg. the fast activity dominated the records. Fast activity was produced by 15 mg. per kg. when given 4 times daily, but not when given as a single dose. After ingestion of toxic doses of the drug fast activity dominated the EEG for the first 26 hours independently of the patient's state of consciousness, but within about 48 hours the EEG had returned to normal. In patients receiving up to 60 mg. per kg. daily the induced fast activity disappeared within 3 weeks despite continued treatment, while the period of time over which fast activity persisted after a single large dose of the drug shortened progressively during a prolonged course of treatment. After abrupt cessation of the drug, clinical withdrawal symptoms and paroxysmal slow activity in the EEG (accentuated by photic stimulation) occurred in 7 out of the 18 patients. These

withdrawal effects were seen after daily doses of 65 mg. per kg. had been continued for one month.

John N. Walton

774. **The Effect of Tranquilizing Drugs and Rehabilitation Activities on Ward Behavior**

A. E. GOLDMAN and H. S. ZAMANSKY. *Journal of Nervous and Mental Disease* [*J. nerv. ment. Dis.*] **129**, 568–572, Dec., 1959 [received Feb., 1960]. 3 refs.

The authors undertook this study to test the hypothesis that the effectiveness of tranquillizing drugs depends to some extent on the total psycho-social environment in which the investigation is carried out. They had previously studied the effect of intensive rehabilitation procedures on 40 female patients suffering from chronic functional psychoses who had been encouraged to engage in special recreational, occupational, educational, and vocational activities during a period of 14 months. At the end of this time tests of their response by means of a " ward behaviour rating scale " showed that the ward behaviour of the rehabilitated patients did not differ significantly from that of controls.

Immediately after the end of the course of rehabilitation 15 patients each from the experimental and the control groups were matched individually on 11 relevant items. Both groups were then given tranquillizing drugs in the form of either chlorpromazine (100 to 200 mg. per day) or reserpine (3 mg. per day) for a median period of 10 months, this being followed by 6 weeks' treatment with placebo tablets and then by 6 weeks without any treatment.

It was found that there was a highly significant improvement in general ward behaviour of the 15 patients given previous rehabilitation. This improvement started after some 3 months' treatment with the tranquillizer and continued during the placebo and the no-treatment periods. In the control group some improvement was maintained after the tranquillizers had been discontinued, but it was not significant. *F. K. Taylor*

775. **The Patient as Listener: a New Dimension in the Structure of Psychotherapy**

K. GEOCARIS. *A.M.A. Archives of General Psychiatry* [*A.M.A. Arch. gen. Psychiat.*] **2**, 81–88, Jan., 1960.

In the author's experience, both with private patients and as director of the psychiatric out-patient clinic, Hillcrest Medical Center, Tulsa, Oklahoma, the demand for psychotherapy exceeds its availability. To meet this need a technique was developed which facilitates psychotherapy yet requires no additional time of the therapist. The method evolved out of the growing practice of playing back tape-recorded therapeutic interviews either to the therapist and patient together or to the therapist himself alone. Because of the increased " dynamic understanding " this yielded it was considered that patients might similarly benefit from listening alone to the recordings. The patients so tested had been receiving " expressive psychotherapy " for hourly sessions once or twice a week. Each session was recorded, and before the next appointment the patient returned to the clinic to listen to the unedited " play-back " of the previous session; when circumstances made this difficult some patients were given the tape to play back at home.

The author reports the results of therapy in 6 cases, one of chronic schizophrenic, one of severe phobic, and 4 of character disorder. While acknowledging the lack of controls and the general difficulties in evaluating and comparing results of psychotherapy, he gained the definite impression that these patients repressed less material, became more quickly aware of their character defences, and developed greater insight. It is stressed that in using this technique caution should be exercised in treating patients with initially high levels of overt anxiety. The method is not intended as a substitute for more intensive psychotherapy, but does seem to increase the effectiveness of therapy given once or twice weekly.

Alan A. Black

776. **An Evaluation of the Effects of Discontinuation of Chlorpromazine**

C. ROTHSTEIN. *New England Journal of Medicine* [*New Engl. J. Med.*] **262**, 67–69, Jan. 14, 1960.

The effect of withdrawal of chlorpromazine from patients who had received the drug for several months and had remained in good condition during that time was studied in 17 patients at the Neuropsychiatric Hospital, Veterans Administration Center, Togas, Maine. All the patients were chronic schizophrenics (average age 45 years) who had shown good hospital adjustment in an open ward and had proved themselves able to cope with a degree of personal responsibility.

Each patient was evaluated for one month on a behaviour-rating scale of 17 items. At the end of that time chlorpromazine was replaced by a placebo and each patient was rated on the same scale twice a week. At monthly intervals thereafter the patient's scores on each variable and on total morbidity were compared with the scores obtained during the observation (chlorpromazine) period. The study was continued for 3 months. Scores of 9 of the 17 variables were largely unchanged during the 3-month period, 2 changed in a negative direction, and 6 showed significant positive changes. The total morbidity scores did not alter significantly. The condition of one patient regressed notably during the trial, and administration of chlorpromazine had to be resumed. Another patient improved sufficiently on the placebo to be able to leave hospital. In the remaining 15 patients there was no significant change during the 3-month period.

The results of this trial suggest that after good hospital adjustment has been achieved with the help of a tranquillizer continuing administration of the drug may not be necessary. *E. H. Johnson*

777. **The So-called Symptomatic Psychoses, Their Place in the System of Psychiatry and Their Psychopathology.** (Die sogenannten symptomatischen Psychosen, ihre Stellung im System der Psychiatrie und ihre psychopathologischen Erscheinungen)

W. SCHEID. *Fortschritte der Neurologie, Psychiatrie und ihrer Grenzgebiete* [*Fortschr. Neurol. Psychiat.*] **28**, 131–144, March, 1960. 19 refs.

Paediatrics

NEONATAL DISORDERS AND PREMATURITY

778. **Endotracheal Aspiration and Oxygenation in Resuscitation of the Newborn**
R. J. H. HODGES, M. E. TUNSTALL, R. F. KNIGHT, and E. J. WILSON. *British Journal of Anaesthesia* [*Brit. J. Anaesth.*] **32**, 9–15, Jan., 1960. 41 refs.

The factors associated with the resuscitation of a group of 137 newborn infants by means of endotracheal intubation, aspiration, and inflation with oxygen are analyzed. There was no evidence of any morbidity associated with this regime, which provides a simple, valuable, and efficient means of achieving early oxygenation, the importance of which is discussed. We stress that the large-scale success of this procedure depends on the use of the correct equipment, favourable departmental organization and the right attitude of mind.—[Authors' summary.]

779. **Some Factors Associated with Neonatal Depression in Operative Obstetrics**
R. J. H. HODGES, E. J. WILSON, R. F. KNIGHT, and M. E. TUNSTALL. *British Journal of Anaesthesia* [*Brit. J. Anaesth.*] **32**, 16–20, Jan., 1960. 3 figs., 12 refs.

Factors associated with postpartum respiratory difficulties in the newborn are examined in a series of 754 operative obstetric deliveries in which 137 infants were intubated after delivery for the purposes of aspiration or intermittent positive pressure inflation with oxygen.

The previous conclusion (Hodges *et al.*, *Brit. J. Anaesth.*, 1959, **31**, 152) that an anaesthetic technique based on thiopentone–suxamethonium and nitrous oxide–oxygen is non-depressant to the infant was further substantiated. The incidence of pre-operative foetal distress causes an overall increase in infant respiratory difficulties irrespective of the operative procedure, be it Caesarean section or forceps delivery. The administration of drugs less than 3 hours before delivery greatly increased the hazard of postpartum respiratory depression in those infants delivered by Caesarean section. The infants in whom for obstetric reasons delivery was delayed for more than 25 minutes after anaesthesia was induced also showed an increased incidence of respiratory difficulties, probably associated with birth trauma. Other factors appeared to be of little significance.—[Authors' summary.]

780. **Similarities of Mechanical Intestinal Obstruction and Aganglionic Megacolon in the Newborn Infant**
O. SWENSON and F. Z. DAVIDSON. *New England Journal of Medicine* [*New Engl. J. Med.*] **262**, 64–67, Jan. 14, 1960. 2 figs., 6 refs.

The diagnosis, clinical features, and treatment of Hirschsprung's disease (aganglionic megacolon) are discussed with reference to 64 cases seen between 1950 and 1958. Of the 64 patients, 47 had the classic signs and symptoms of intestinal obstruction, abdominal distension, intractable constipation, and vomiting. Clinically no distinction can be made between these symptoms and those of ileal atresia. Barium-enema examination will demonstrate the distended colon, thus showing that there is no small bowel obstruction, but in the present series 4 false positive radiographs were obtained following such examination. The authors consider that rectal biopsy, which reveals the presence or absence of ganglion cells, is the only reliable diagnostic method. Unnecessary exploration of newborn infants with Hirschsprung's disease in whom obstruction of the small intestine has been mistakenly diagnosed has in the past been associated with a high death rate and should be avoided by barium-enema examination. The death rate from one-stage resection has been reported to be between 33% and 50%. Colostomy performed when enterocolitis has developed does not give good results, "intensive medical treatment" being more successful than surgery at this stage. The best results are obtained by colostomy immediately the diagnosis is established, resection of the aganglionic segment being delayed until the child weighs 20 to 30 lb. (9·1 to 13·6 kg.). *E. H. Johnson*

781. **The Blood Volume of Infants. III. Alterations in the First Hours after Birth**
T. R. C. SISSON and L. E. WHALEN. *Journal of Pediatrics* [*J. Pediat.*] **56**, 43–47, Jan., 1960. 1 fig., 10 refs.

The authors of this paper from the University of Rochester, New York, report a study of the changes in the blood volume of infants in the first few hours of life. The total blood plasma and erythrocyte volumes, the haemoglobin concentration, and the venous haematocrit were determined in 12 normal full-term infants by a technique previously described (Sisson *et al.*, *J. Pediat.*, 1959, **55**, 163), blood being taken for this purpose within an hour of birth and again at 3, 4, or 5 hours. The mean total blood volume was 88 ml. per kg. body weight within one hour of birth and had risen to 107 ml. per kg. between 3 and 5 hours; the mean plasma volume was 50 ml. per kg. initially and 60 ml. per kg. after 3 to 5 hours; the mean erythrocyte volume increased from 38 to 47 ml. per kg. in the same period. These results suggest that attempts to increase the infant's blood volume by milking the umbilical cord and thus increasing the haemodynamic changes described might cause circulatory embarrassment. In a discussion the authors state that their findings do not support those of Gairdner *et al.* (*Arch. Dis. Childh.*, 1958, **33**, 489; *Abstr. Wld Med.*, 1959, **25**, 366), who considered that a shift of plasma from the vascular compartment occurred shortly after birth, basing this conclusion, however, on a comparison of cord blood samples and blood taken from the infant a few hours after delivery. *R. M. Todd*

782. **Cold Injury in the Newborn**
B. D. Bower, L. F. Jones, and M. M. Weeks. *British Medical Journal* [*Brit. med. J.*] **1**, 303–309, Jan. 30, 1960. 4 figs., 14 refs.

The clinical features of cold injury in the newborn were fully described by Mann in 1955, and since then this condition has been more frequently recognized. A retrospective survey at the Children's Hospital, Birmingham, showed that between 1946 and 1956, 183 newborn infants were admitted with a temperature of 95° F. (35° C.) or lower. The cause of the low temperature was considered to be primary cold injury in 70 patients (42 male and 28 female), but prematurity (48), cerebral birth injury (23), asphyxia (9), and severe infections (15) were among the other common causes. The symptoms in the infants with primary cold injury in order of frequency were refusal of feeds, swelling of the limbs, coldness to touch, lethargy, vomiting, oliguria, redness of the skin, and jaundice. At the time of admission to hospital the commonest clinical features were oedema, immobility, sclerema, and redness of the face. The most important aetiological factor was a low environmental temperature; the external temperature recorded at Edgbaston Observatory at the time 53 of the 70 infants were admitted was below 35° F. (1·7° C.). However, 7 infants were admitted when the external temperature was 44° F. (6·7° C.) or higher, but the signs and symptoms in these patients were typical of cold injury. Other aetiological factors considered important were insufficient clothing or tight wrapping ("concooning") of the infant, which restricts physical activity.

The prevention of neonatal cold injury demands an awareness of the danger of exposure to cold on the part of all who handle the infants. When the condition is established the aim of treatment should be to disturb the infant as little as possible, to raise the body temperature gradually over a period of several days, and to ensure an adequate oxygen intake; antibiotics should be given prophylactically. Of the 70 infants in this series, 18 died; post-mortem examination in 15 revealed pulmonary haemorrhage and infective lesions. Follow-up information concerning 36 of 52 survivors showed that general growth was normal except in one child with acyanotic congenital heart disease; in 2 there was mild mental retardation and in one spastic quadriplegia with gross mental retardation. *R. M. Todd*

783. **Experimental and Clinical Studies of the Prophylaxis of Kernicterus in Premature Infants with Prednisone.** (Experimentelle und klinische Untersuchungen zur Prophylaxe des Kernikterus von Frühgeborenen mit Prednison)
H. Wiesener. *Monatsschrift für Kinderheilkunde* [*Mschr. Kinderheilk.*] **108**, 1–5, Jan., 1960. 37 refs.

The serum bilirubin concentration in 25 healthy full-term infants and in 74 premature infants was determined by the author at the Paediatric Clinic of the Free University of Berlin. In the full-term infants the value rose steeply to an average of 5 mg. per 100 ml. on the 4th day of life and then fell slowly to reach 2 mg. per 100 ml. on the 14th. In the premature group peak concentrations were reached on the 6th day, a mean value of 10 mg. per 100 ml. being obtained in infants under 1,500 g. in weight and of 9 mg. per 100 ml. in those over 1,500 g., these values falling to 2 mg. per 100 ml. in the 6th week in the former group but in the 4th week in the heavier infants. Traces of indirect bilirubin were present in the urine of 11 premature infants, but no indirect bilirubins were detected. A study of the amount of bilirubin excreted in the faeces showed that none of the full-term infants excreted bilirubin after the 3rd week, but premature infants continued to do so until the 8th week. When 10 mg. of prednisone daily was administered faecal excretion of bilirubin rose to between 6 and 8 mg. daily and direct bilirubins were detected in the urine.

The author now gives prednisone prophylactically to prevent the hyperbilirubinaemia which is usually present in the kernicterus of prematurity, employing a dosage of 2·5 mg. four times daily in conjunction with tetracycline, 20 to 40 mg. per kg. body weight over a period of 7 days. In rare cases of long-lasting jaundice a reduced daily dose of 2 to 5 mg. of prednisone may be given for 2 to 3 weeks. He recommends that prednisone be given to all premature infants weighing less than 1,000 g. from the first day of life. Because there is no correlation between the intensity of jaundice and the degree of bilirubinaemia the serum bilirubin concentration should be determined on the 2nd, 4th, and 6th days in any premature infant who becomes jaundiced, and prednisone should be given at once if this level rises to 15 mg. per 100 ml. on the 4th day because of the danger of the sensitive brain cells being affected by the toxic action of bilirubin, although kernicterus may not necessarily develop. If on the 4th day the value is 20 mg. per 100 ml. or higher exchange transfusion is essential. In borderline cases the clinical picture may be more important than laboratory tests, for bilirubinencephalopathy with apnoeic phases has been reported in infants with relatively low serum bilirubin concentrations; but in such cases little benefit is likely to be obtained with prednisone. The author's tabulated statistics and graphs show that the mortality from kernicterus due to prematurity has been reduced to *nil* since the introduction of prophylaxis with prednisone. *E. S. Wyder*

CLINICAL PAEDIATRICS

784. **Developmental Posterior Enteric Remnants and Spinal Malformations: the Split Notochord Syndrome**
J. F. R. Bentley and J. R. Smith. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **35**, 76–86, Feb. [received April], 1960. 21 figs., 38 refs.

Writing from the Royal Hospital for Sick Children, Glasgow, the authors describe the malformations that may arise from a split notochord, with herniation of gut anlage endoderm through the gap in the notochord out to the dorsal ectoderm. The latter may rupture, giving rise to a fistula between the yolk sac and the amniotic cavity.

The malformations of the viscera of the chest or abdomen that may arise from the herniated gut are posterior

enteric fistulae, sinuses, diverticula, and cysts, according to whether the whole fistula persists or only its dorsal part, ventral part, or an intermediate part. The remnants may undergo hamartomatous malformation. In the spinal and central nervous system the resulting malformations may include a complete anterior and posterior spina bifida, an anterior spina bifida only, a posterior spina bifida only, diastematomyelia with fusion of the medial hemivertebral pedicles, or diplomyelia. The authors describe in detail 5 illustrative cases and discuss the embryological mechanisms which may result in a split notochord. *C. O. Carter*

785. **Accessory Enteric Formations: a Classification and Nomenclature**
J. R. SMITH. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **35**, 87–89, Feb. [received April], 1960. 2 figs., 8 refs.

The author proposes a new classification of accessory formations of the gut, which have hitherto been given various designations such as enterogenous cysts, archenteric cysts, gastro-thoracic cysts, and duplications. He proposes three main groups: (1) duplications, (2) vitelline remnants, (3) dorsal enteric remnants.

(1) The criterion for a " duplication " is that it should lie adjacent to, and share a common blood supply (and usually also a common muscle coat) with normal gut. These abnormal structures, which may be spherical or tubular, are thought to originate from the coalescence of a group of vacuoles within the thickened epithelium of the more rapidly developing embryonic gut wall which have failed to rupture into the normal lumen of the gut. (2) " Vitelline remnants " represent failure of closure of the vitello-intestinal duct, and may be subdivided into vitelline fistula, sinus, cyst, and diverticulum. (3) " Dorsal enteric remnants " are thought to be remnants of an abnormal fistula between the yolk-sac and the amniotic cavity passing through the notochord. This fistula may leave remnants which can be described as dorsal enteric fistula, sinus, cyst, or diverticulum. There may be varying degrees of concomitant vertebral anomaly with diastematomyelia or diplomyelia. *C. O. Carter*

786. **Biochemical Studies in Idiopathic Hypercalcaemia of Infancy**
J. O. FORFAR, S. L. TOMPSETT, and W. FORSHALL. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **34**, 525–537, Dec., 1959 [received Feb., 1960]. 2 figs., 37 refs.

The authors report, from the University and Northern Group of Hospitals, Edinburgh, the results of estimating, first in 110 normal infants, the serum calcium and serum total and free cholesterol levels, from which they calculated that of serum cholesterol esters. The serum calcium level was determined in 65 cases by the method of Kramer and Tisdall and in 45 by the method of Trinder. The latter method gave a slightly lower mean figure, 9·9 mg. per 100 ml. (43 cases) as opposed to 10·3 mg. per 100 ml. (61 cases) by the former. The methods of determining the serum total and free cholesterol levels are described. The means, standard deviations, and ranges of all values are tabulated, as well as the individual results. Also the products for the values of calcium × total cholesterol, calcium × free cholesterol, and calcium × cholesterol esters are given, since these may be significant in hypercalcaemia.

They then studied the relationship between the serum calcium and serum cholesterol levels in 20 cases of idiopathic hypercalcaemia of infancy, again detailing the individual results. A significant positive correlation between the serum calcium level and both the total and free cholesterol levels was demonstrated. The value for cholesterol esters, however, did not vary with the serum calcium level. In certain cases of this disease in which the serum calcium level was equivocal or might have fallen the raised serum cholesterol level was of diagnostic value, and the product of serum calcium level multiplied by serum cholesterol level was then significant. Since certain cholesterol derivatives exert a vitamin-D-like activity the authors suggest that this disease may be primarily one of cholesterol metabolism.

Lastly, using the method of Taylor (*Biochem. J.*, 1953, **54**, 48) the authors established the serum citrate level in 32 normal infants aged 2 to 15 months. The mean for this value was 2·4 mg. per 100 ml. (range 1·2 to 3·5 mg. per 100 ml.). In 28 infants suffering from idiopathic hypercalcaemia simultaneous estimations of the serum calcium, serum citrate, and urinary citrate levels showed that the mean value did not differ from normal, but the range was wider (0·6 to 4·8 mg. per 100 ml.). During the active stage of the disease, however, the serum citrate and urinary citrate levels were low, but rose during recovery, a significant negative correlation between the serum calcium and citrate levels being demonstrated during the active phase of the disease. They point out that these findings are at variance with the usual interpretation of idiopathic hypercalcaemia of infancy as being due to an excess of a vitamin-D-like substance, for vitamin D normally raises the serum and urinary citrate levels. This may not be true, however, in patients of the age at which idiopathic hypercalcaemia occurs, and a case is cited from the literature in which vitamin-D intoxication in an infant led to lowered serum and urinary citrate levels. *H. G. Farquhar*

787. **Intravenous Fluid Therapy for Infants and Children: Physiologic Principles and a Practical Regimen with Examples of Application.** [Review Article]
E. BRUCK, T. ACETO JR., and C. U. LOWE. *Pediatrics* [*Pediatrics*] **25**, 496–516, March, 1960. 7 figs., bibliography.

788. **Osteomyelitis of the Superior Maxilla in Infants: a Report on 24 Personally Treated Cases**
F. CAVANAGH. *British Medical Journal* [*Brit. med. J.*] **1**, 468–472, Feb. 13, 1960. 10 figs., bibliography.

Although only 152 cases of osteomyelitis of the superior maxilla in infants have been reported in the literature since the condition was first described by Rees in 1847, the author has seen and treated 24 such cases over a period of 17 years. It is emphasized that unless the condition is diagnosed promptly and treated ade-

quately not only may the mortality be high, but the morbidity may be disastrous, with asymmetry of the face, chronically discharging sinuses and fistulae with sequestration of the superior maxilla, ectropion, and loss of teeth.

Bacteriologically, the infecting organism in the majority of cases is *Staphylococcus aureus*. The author discusses the source of the infection and the site of onset, both of which are doubtful. The diagnosis is not difficult provided the condition is borne in mind. It should be suspected in an infant with sudden onset of swelling of one eye, pus in the nostril, and swelling of the alveolus on the affected side. Gentle pressure over the cheek will produce a flow of pus from the nostril or from a sinus in the alveolus. X-ray examination is very little help at this stage. The prognosis is good with early treatment, which consists in administration of the appropriate antibiotic and draining the abscess through the nose. A trocar is inserted into the antrum and a " polythene " tube is then passed through it, left *in situ*, and used for irrigating the antrum with saline and instilling the antibiotic. The tube remains in position until no pus has been obtained for 2 or 3 days. If the polythene tube falls out it is quite easily replaced. The average stay in hospital of the affected infants is 10 days. Four illustrative cases are briefly described and well illustrated.

[This paper is of great importance and value, since the condition is not adequately dealt with in the textbooks; it should be read in full.]

Andrew M. Desmond

789. **Childhood Peptic Ulcer**

A. MUGGIA and H. M. SPIRO. *Gastroenterology* [*Gastroenterology*] **37**, 715–724, Dec., 1959. 31 refs.

The authors review the clinical course of peptic ulceration in children with reference to 24 patients (20 male and 4 female) under the age of 16 seen at Yale–New Haven Medical Center, Connecticut. Duodenal ulcers were present in 21 of the patients and gastric ulcers in only 3. The authors state that the manifestations of peptic ulcer in children differ according to age at onset; the cases are therefore divided into four groups. In Group 1, neonatal, the commonest presenting feature is a sudden haematemesis or melaena and, on occasions, perforation; the ulcer either heals rapidly or leads equally quickly to death. In Group 2, infantile (up to 2 years of age), the commonest presenting feature is also haematemesis or melaena, but other signs such as ill-defined abdominal pain, failure to thrive, intermittent vomiting, and diarrhoea also occur. In this group the diagnosis of peptic ulcer is rarely considered in the absence of melaena and, in the authors' view, is " usually blundered upon ". In Group 3, early childhood (2 to 9 years), the characteristic feature is recurring abdominal pain which is frequently epigastric, is not relieved by food, and is often associated with behaviour problems; vomiting is common. In Group 4, late childhood, the symptomatology is almost identical with that seen in adults with the possible exception of a higher incidence of haemorrhage.

It is emphasized that awareness not only of the occurrence of peptic ulcer in children but also of its atypical symptomatology is necessary if serious complications and death are to be avoided. Treatment should be conservative, if possible, and the dietary regimen should aim at frequent meals rather than the specific avoidance of " bad " foods, such a " positive permissive approach " being better for the children than a " restrictive negative " one. Antispasmodics and antacids should be avoided. Adjustment, if necessary, of the home environment of the child is an important factor in treatment. The authors consider that most of their patients developed an ulcer in a setting of conflict or as a result of a feeling of insecurity, but they admit that no fundamental personality trait is associated with peptic ulceration. Surgical treatment should be reserved for cases of massive haemorrhage or perforation and every effort should be made to avoid operation in children under the age of 16.

J. Warwick Buckler

790. **The Hyperkinetic Type of Infantile " Toxicosis " [Toxic Gastro-enteritis].** (Über die hypermotile Form der Säuglings-" Toxikose ")

P. G. KISS. *Annales paediatrici* [*Ann. paediat.* (*Basel*)] **194**, 11–36, Jan., 1960. 13 refs.

The author divides the cases of infantile toxicosis (toxic gastro-enteritis) into two types: (*a*) the stuporose-comatose, and (*b*) the hyperkinetic type. The symptomatology of the hyperkinetic type is described and the differential diagnosis of the two forms discussed. A detailed account is given of the aetiology and pathogenesis of the hyperkinetic form. The disease process usually starts in the invasive phase of other acute infectious diseases. The whole of the infantile body develops a state of psycho-motor-vegetative unrest. A severe degree of tachycardia supervenes which leads after a time to an acute coronary insufficiency and in turn to hypoxia and myocardial damage, hypodiastolic and dynamic cardiac insufficiency. In turn this results in hypoxia, hypercapnia and congestive oedema in various organ systems. The tissue cells enter into a state of anergy, which may be the immediate cause of death in the fatal cases.

Treatment is discussed in full. Contrary to the previously generally fatal outcome, cases recognized in time can now be cured with certainty.—[Editorial summary.]

791. **Eosinophilia in Children with Asthma and Bronchiectasis**

L. B. STRANG. *British Medical Journal* [*Brit. med. J.*] **1**, 167–169, Jan. 16, 1960. 2 figs., 10 refs.

In this paper from King's College, University of Durham, a study is reported of the incidence and characteristics of eosinophilia in children with asthma and bronchiectasis. The eosinophil count was determined initially and then serially at routine out-patient attendances of 43 asthmatic children and 40 suffering from bronchiectasis. Forced expiratory volume in one second ($F.E.V._1$), which the author has found to be a satisfactory objective measurement of ventilatory capacity and thus of the severity of the asthma, was measured at intervals for 6 months in 14 asthmatics and correlated

with the eosinophil count. In 37 of the 43 asthmatics the blood eosinophil count was more than 600 per c.mm.; none of the 40 patients with bronchiectasis had eosinophilia. Serial determinations showed that the eosinophilia was very persistent. It was not related to the F.E.V.$_1$ or to the severity of the asthma. Since the eosinophil count was not raised in the patients with bronchiectasis the author suggests that it may serve as a means of distinguishing the two conditions in borderline cases. *Winston Turner*

792. **"The Coughing Disease" in Children**
R. GRENVILLE-MATHERS. *British Journal of Diseases of the Chest* [*Brit. J. Dis. Chest*] **54**, 72–77, Jan., 1960. 1 fig., 12 refs.

The author analyses the findings in 2,442 children referred to the Harrow Chest Clinic between 1955 and 1957 because of respiratory symptoms, cough being one of the symptoms in the majority. In 675 patients further investigation was required, the findings being as follows: non-respiratory illness, 152; tuberculosis (including non-respiratory forms), 89; a single acute respiratory infection of short duration, 69; respiratory infection of prolonged duration, 213; recurrent bronchitis, 100; allergic asthma, 42; and bronchiectasis, 10.

Treatment was on simple lines; the cough was controlled by raising the foot of the bed and recurrent bronchitis and bronchospasm responded to breathing exercises. Antibiotics were given only when symptoms were severe. Allergic manifestations tended to persist, but other respiratory ailments did not appear to be the precursors of adult chronic respiratory disease.
B. Golberg

793. **The Effect of a Bronchodilator Aerosol on Ventilatory Capacity in Fibrocystic Disease of the Pancreas**
B. GANDEVIA and C. ANDERSON. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **34**, 511–515, Dec., 1959 [received Feb., 1960]. 8 refs.

In this study, carried out at the Royal Children's Hospital, Melbourne, the authors' purpose was to assess the value of an aerosol of 1:1,000 *iso*propyl-noradrenaline (isoprenaline) in the treatment of the wheezing which is a relatively common symptom in fibrocystic disease of the pancreas. Using a spirometer they assessed the vital capacity (V.C.) and the forced expiratory volume in one second (F.E.V.$_1$), this being recorded on a kymograph. The percentage of the vital capacity expired in the first second was then calculated (F.E.V.$_1$%). A mean of three readings was taken and compared with those in normal children, comparison being based on height and not on age, since patients with this disease are often of small stature. The aerosol was then administered for 1½ to 2 minutes and the same respiratory measurements repeated.

The 16 children with fibrocystic disease of the pancreas were divided into three groups of 5, 6, and 5 patients respectively, according to the severity of their respiratory symptoms. Before aerosol therapy these children had a normal or lowered V.C. and a reduced F.E.V.$_1$ and F.E.V.$_1$%, the obstructive ventilatory defect correlating well with the clinical assessment and increasing progressively from Group 1 to Group 3. After aerosol therapy there was a consistent improvement which was most marked in the middle group of 6 patients, but with some exceptions the F.E.V.$_1$% did not improve. The authors attribute this to the fact that besides reversible bronchospasm there are other causes of respiratory obstruction in fibrocystic disease of the pancreas, including secretions in the bronchi, organic narrowing of the bronchi, and emphysema. They conclude that an aerosol of isoprenaline may be of value in these cases and are currently undertaking a long-term trial. Relevantly, they point out that their tests did not assess the value of bronchodilator drugs in facilitating the expulsion of bronchial secretions by coughing. The detailed results of the pulmonary tests are tabulated and brief case histories are presented. *H. G. Farquhar*

794. **Long-term Prognosis of the Nephrotic Syndrome in Children.** (Pronostic éloigné du syndrome néphrotique de l'enfant)
R. DEBRÉ, J. MARIE, P. ROYER, B. LÉVÊQUE, and L. KAPLAN. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **36**, 531–544, Feb. 24, 1960. 5 figs., 22 refs.

The authors report the long-term results in 128 boys and 65 girls suffering from the nephrotic syndrome who were treated at the Hôpital des Enfants-Malades, Paris, between 1927 and 1958, 97 being between the ages of 2 and 5 years. Of these the authors have been able to follow up 174, whom they divided into 4 groups: (1) 34 children treated from 1927 to 1944 before the introduction of antibiotics; (2) 36 who were treated with sulphonamides and antibiotics between 1944 and 1951; (3) 68 treated from 1951 to 1955 with antibiotics and one or more courses lasting 10 to 15 days of ACTH or cortisone; and (4) 55 children treated from 1955 onwards who, in addition to antibiotics, received a primary course lasting 10 to 15 days of either ACTH (75 to 150 mg. daily), cortisone (100 to 300 mg. daily), or prednisone (20 to 60 mg. daily), followed by courses of corticotherapy on 3 or 4 days of each week for a minimum of 4 months, and longer in patients who had relapsed or who failed to go into remission. The recovery rates in the four groups were 29%, 52%, 53%, and 63% respectively, while sequelae such as albuminuria, haematuria, and azotaemia occurred in 3%, 8%, 14%, and 20% respectively. In Group 1 the over-all mortality was 67% (27% from infection and 40% from renal failure), in Group 2 it was 40% (12% from infection and 28% from renal failure), in Group 3 33% (2% from infection and 31% from renal failure), and in Group 4 16% (*nil* from infection and 16% from renal failure).

The authors conclude as follows. (1) Although twice as many boys as girls suffer from the nephrotic syndrome, sex is not prognostically important. (2) The age of onset of the condition, while most commonly between 2 and 5 years, is of no prognostic significance. (3) When the syndrome occurs as a familial tendency the prognosis is very bad, and indeed all 6 of their patients in this group died. (4) The association of haematuria, azotaemia, and hypertension with nephrosis worsens the

outlook in general, but by no means inevitably in individual cases. Modern treatment of the nephrotic syndrome has indubitably contributed to a more favourable prognosis, this study showing that antibiotics have reduced the mortality from infection from 27% in 1927 to *nil* in 1959. The authors were unable to find any evidence, however, that corticotherapy in short courses has influenced the long-term prognosis. Moreover, they are cautious in claiming too much for the obvious and immediate benefit of prolonged corticotherapy in enabling nephrotic patients to lead a more normal life than was previously possible. They consider that a true assessment of corticotherapy will not be possible for many years, since in many cases insufficient time has elapsed since treatment was completed, many others still remain under treatment, and the beneficial influence of antibiotics and of newer knowledge of electrolytic changes in nephrosis cannot yet be sufficiently separated from that of corticotherapy. *E. S. Wyder*

795. **Thrombotic Microangiopathy of the Kidney in Children.** (La microangiopathie thrombotique du rein chez l'enfant)

P. ROYER, R. HABIB, and H. MATHIEU. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] 36, 572–587, Feb. 24, 1960. 10 figs., bibliography.

The authors discuss the syndrome seen in infancy, and known under various names, in which haemolytic anaemia, acute nephropathy, and, less constantly, thrombocytopenic purpura and neurological anomalies are associated. Anatomically three forms of nephropathy occur: (1) Moschowitz's thrombotic microangiopathy affecting all organs of the body, including the kidney; (2) thrombotic microangiopathy affecting the kidney alone; and (3) Gasser's thrombotic microangiopathy of extrarenal organs associated with bilateral symmetrical necrosis of the renal cortex. On the basis of 8 cases of the syndrome seen recently at the Hôpital des Enfants-Malades, Paris, the authors describe in detail the history and the clinical and histo-pathological findings [with excellent illustrations] in one case of the first form, 4 of the second, and 2 of the third; the 8th case is included as an example of a curable form of nephropathy which has been recognized on clinical and haematological grounds, but for which histo-pathological proof is lacking. The authors consider that all 4 forms should be considered as manifestations of thrombotic microangiopathy of the kidney. Of their 8 cases, 6 occurred in boys, and the patients' ages ranged from 5 months to 11 years.

Renal involvement may be recognized by (1) the finding of macroscopic and microscopic haematuria and marked albuminuria, a raised blood urea level with hypochloraemia, hyponatraemia, and hypocalaemia, and terminal oedema and hypertension; (2) the presence of the nephrotic syndrome, and oedema; and (3) the occurrence of acute anuria. Of the haematological components of the syndrome, haemolytic anaemia is constantly, and thrombocytopenic purpura inconstantly, present. The anaemia is sudden in onset and occurs at the same time as and in close relationship with the nephropathy; it is normochromic in type, with fragmentation and distortion of the erythrocytes. Blood transfusion does nothing to improve the anaemia, and the transfused erythrocytes survive for only a short period. Thrombocytopenic purpura was present in addition in 3 of the 8 cases. Thrombotic microangiopathy is always ushered in by vomiting, sometimes accompanied by abdominal pain and melaena and less often by diarrhoea. The temperature is usually normal or slightly elevated. Enlargement of the liver, spleen, or lymph nodes is uncommon. Convulsions are frequent and somnolence precedes death. Careful investigations shed no light on the aetiology of the condition. Of the 8 patients, 7 died within 5 days to 8 weeks of the onset of thrombotic microangiopathy despite administration of antibiotics, corticotherapy, blood transfusions, and total exchange transfusions. *E. S. Wyder*

796. **Functional Microangiopathy of the Kidney in Treated Diabetes Mellitus in Childhood.** (Funktionelle Mikroangiopathie der Nieren beim behandelten Diabetes mellitus im Kindesalter)

G. STALDER, R. SCHMID, and M. VON WOLFF. *Deutsche medizinische Wochenschrift* [*Dtsch. med. Wschr.*] 85, 346–350, Feb. 26, 1960. 3 figs., 37 refs.

The renal complications of diabetes mellitus, apart from inflammatory disease, include functional nephropathy due to dehydration occurring as a pre-renal azotaemia in diabetic coma, and diabetic nephropathy due to arteriosclerosis, as in the intercapillary glomerulofibrosis of the Kimmelstiel–Wilson syndrome. Nephropathy is clinically recognizable only in adults, yet 50% of deaths among juvenile diabetics are due to renal causes, and as the treatment of infection and coma improves so will renal failure account for an even higher proportion of the deaths.

In the study here reported from the University Paediatric Clinic, Basle, the authors set out to discover evidence of renal damage in juvenile diabetic patients which might predispose them to nephropathy. Inulin clearance tests performed on 46 healthy children and 18 diabetic patients under the age of 20 years showed that the mean volume of plasma cleared of inulin per minute in the control group was 121 ml., whereas in the diabetics it was 169 ml., being over 200 ml. in 5 of these. On the basis of these results and other findings the authors suggest that in juvenile diabetics it is indeed possible to speak of a functional renal microangiopathy, which is characterized by (1) an increased rate of glomerular filtration, (2) functional hypertrophy of the epithelium of the proximal tubules, and (3) remarkable fluctuations in the effective renal blood flow. They consider moreover that in this condition both the intraglomerular filtration pressure and the permeability of the glomerular capillary wall are increased, and that these increases, together with abnormal fluctuations in the tone of the afferent and efferent arterioles, cause pathological pressure changes to occur in the glomerular capillaries. In their experience this condition appears to be unrelated to the age of the patient, the duration of the symptoms, or the type of insulin used in treatment. There is some correlation,

however, between the condition and the degree of diabetic decompensation, with or without ketosis.

The authors conclude by advancing the hypothesis that if functional renal microangiopathy has been present for a number of years it might be an important aetiological factor in the production of intercapillary glomerulofibrosis. They point out also that if their hypothesis can be confirmed the inulin clearance test would be not only of prognostic value in juvenile diabetics, but would also be an aid in the prophylaxis of nephropathy when assessing the ability of vasoactive drugs to reduce intraglomerular pressure.

E. S. Wyder

797. **Central Hemorrhagic Encephalopathy of Early Infancy**
C. B. COURVILLE. *Neurology* [*Neurology (Minneap.)*] **10**, 70–80, Jan., 1960. 3 figs., 38 refs.

This study is based upon 3 cases of acute generalized hemorrhagic necrosis of the cerebral centrum of early infancy. The lesions were so severe as to be incompatible with life for more than a few hours. From clinical information present in each instance, it seems logical to conclude that acute anoxemia was the primary cause. This conclusion seems reasonable because, in many instances of acute severe cerebral anoxia, numerous petechial hemorrhages are found in the white matter of the brain. The remarkable similarity of the distribution of the acute lesions in these 3 instances to that of the structural changes found in the so-called chronic cystic degeneration of the cerebral centrum found in infants raises a question of the possible relation of cause and effect of the two. This possible connection is considered in some detail and the question of anoxemia or some gross impairment of the fetal circulation associated with the birth process is reviewed. The most likely answer to this question seems to lie in this possibility.—[Author's summary.]

798. **Postnatal Arrest of Development of the Brain and Its Regression.** (Postnataler Stillstand der Entwicklung des Gehirns und seine Entwicklungsregression)
I. LESNÝ and F. DITTRICH. *Zeitschrift für Kinderpsychiatrie* [*Z. Kinderpsychiat.*] **27**, 1–6, Jan., 1960.

At the Neurological Clinic, Prague, the authors observed 5 children whose physical and mental development appeared normal up to 3 months to 2 years of age, but then suddenly ceased and often actually regressed. This was usually a sequel to head injury or infection. Convulsions and severe neurological lesions, such as spastic quadriplegia, developed subsequently. The first child was 7 months old when he became ill and eventually died aged 21 months after a convulsion. The necropsy showed a hypoplasia of the brain, which corresponded in size to that of a child of 6 months. There were no other lesions. The second child was normal up to 2½ years, but sustained a head injury when one year old. From the age of 2½ he suffered from grand mal epilepsy and progressive mental retardation. At the age of 8 his I.Q. was below 25 and his electroencephalogram showed gross evidence of epilepsy. The third child developed normally up to 2 years when he sustained a head injury. He became grossly retarded, with spastic quadriplegia. He died at 3 years of age. At necropsy premature synostosis of the sagittal sutures and hypoplasia of the brain (which corresponded in size to that of a 4-month-old baby) was found. The fourth child developed normally for 20 months. After a sore throat gradual neurological deterioration followed, with the development of a pontine syndrome. The electroencephalogram was of infantile pattern and air encephalography showed hydrocephalus. At the age of 2½ he was grossly retarded and had spastic quadriplegia and epilepsy. He died at home later. The fifth child developed normally up to 2 years. After an attach of mumps his development became arrested and later regressed. He developed a spastic paraplegia, and air encephalography showed diffuse brain atrophy. By the age of 5 he was blind, unable to sit, and had quadriplegia. The electroencephalogram showed a grossly abnormal pattern. The authors believe that these cases are unique in the literature, as similar clinical pictures in the past were usually attributed to prenatal causes.

[This group of cases is not altogether homogenous. No reference is made to " hypsarrhythmia " or " infantile spasms ", in which condition normal early development is usually followed by gross intellectual regression not unlike that recorded in this paper.] *John Lorber*

799. **The Postconcussion Syndrome in Children.** [In English]
U. OTTO. *Zeitschrift für Kinderpsychiatrie* [*Z. Kinderpsychiat.*] **27**, 6–20, Jan., 1960. 6 figs.

To determine whether previous head injury plays any part in the causation of mental symptoms in children the author surveyed the case histories of 3,588 children referred to the Child Psychiatric Clinic of the Crown Princess Lovisa's Hospital for Children, Stockholm. Only 29 were diagnosed as suffering from a post-concussion syndrome. The number of children with a history of previous head injury was much larger, amounting to 124 out of 620 children who were admitted as in-patients for treatment; 46 of these had been unconscious. In one-third of the cases the head injury occurred before the age of 3½ years. They were commoner and more severe in boys. The most important symptoms which had developed in these children several years after the accident were aggressiveness, destructiveness, hyperactivity, emotional instability, affective outbursts, a tendency to exaggerated persistence, poor powers of concentration, and deterioration of memory. In many instances important symptoms of a psychiatric nature were already present before the head injury and there were also important hereditary and other environmental factors. The electroencephalogram was abnormal in three-quarters of the children with post-concussion syndrome, particularly if objective neurological signs were also present. The author has considerable doubt about the importance of head injury as such in the causation of symptoms developing subsequently, and feels that in judging an individual case more precise investigations would be necessary than are available at present.

John Lorber

Public Health

800. **Housing as an Environmental Factor in Mental Health: the Johns Hopkins Longitudinal Study**
D. M. WILNER, R. P. WALKLEY, J. M. SCHRAM, T. C. PINKERTON, and M. TAYBACK. *American Journal of Public Health* [*Amer. J. publ. Hlth*] **50**, 55–63, Jan., 1960. 3 refs.

This paper from the Johns Hopkins University, Baltimore, presents the preliminary findings after 18 months of a study of the effects of improved housing on social adjustment and mental health. [A preliminary report on the effects on morbidity was given in a previous paper (Wilner *et al.*, *Amer. J. publ. Hlth*, 1958, **48**, 1607; *Abstr. Wld Med.*, 1959, **25**, 452).] Approximately 400 negro families (2,000 persons) who were transferred from a slum area to a new housing estate were compared before and after the move with approximately 600 families (3,000 persons), comparable initially in the distribution of all demographic variables studied, who remained in the slum area. Comparison of initial housing quality by the combination of individual items into a weighted index, however, showed that almost 10% more test than control families were to be found in " very bad " housing. The initial morbidity data demonstrated a close comparability of the two groups in respect of medical history and incidence of illness in the 2 months before the interview. During the first 18 months of the study period, after a small initial reversal, the illness rates in the test group remained slightly lower than those in the control group.

The results of the present study support to some extent many of the hypotheses of the investigation: the test families unquestionably showed an awareness of their improved circumstances, and their reports of behaviour and attitude confirmed speculation that space in and of itself is an important factor. Improved housing also consistently increased the activities which the family undertakes together. The most conspicuous finding was the marked increase in neighbourly interactivity, a fact which is attributed as much to architecture as to improved housing quality. There was less confirmation of basic hypotheses concerning individual self-assignment to a position in the social class hierarchy. It appears that the size of the change in housing quality is an important consideration in the evaluation of the effect of housing; another consideration of obvious importance is the length of residence in the particular dwelling unit.

R. G. Meyer

801. **Cleansing and Sterilization of Hospital Blankets**
C. G. A. THOMAS, B. WEST, and H. BESSER. *Guy's Hospital Reports* [*Guy's Hosp. Rep.*] **108**, 446–463, 1959. 12 refs.

Working at Guy's Hospital Medical School, London, the authors studied various washing agents to assess their suitability for routine cleansing of hospital blankets, and also the sterilizing effects of formaldehyde vapour, ethylene oxide, and boiling against normal degrees of contamination and against gross contamination produced by impregnating blanket material with known organisms grown on solid media.

Blankets were still heavily contaminated after being laundered with soap flakes. The bacterial counts were found to be lower after the blankets were laundered with anionic detergents, but 17% of them remained contaminated with *Staphylococcus aureus*. The best results were obtained with mixtures of non-ionic detergents and quaternary ammonium compounds, all three such preparations tried removing over 99% of the organisms originally present, including *Staph. aureus*. Many of the sweep-plates used to sample the laundered blankets remained sterile. The blankets did not become matted or felted and it was considered that blankets could be washed with these agents many times without significant deterioration in quality.

Using a standard commercial machine and a commercial preparation of formaldehyde [precise composition not disclosed] the authors found that freely exposed blanket surfaces were sterilized but organisms on test strips sandwiched between two layers of blanket often survived. [The effect of preliminary evacuation of the sterilizing chamber was not tried.] Sterilization was slow and *Staph. aureus* survived one hour's exposure to ethylene oxide at concentrations of 5 to 14% by volume. Boiling for 5 minutes removed vegetative but not spore-forming organisms from blankets without grossly damaging the blanket material. More prolonged boiling caused shrinkage and progressive loss of texture.

H. Caplan

802. **The Effect of Chlorine in Water on Enteric Viruses. II. The Effect of Combined Chlorine on Poliomyelitis and Coxsackie Viruses**
S. M. KELLY and W. W. SANDERSON. *American Journal of Public Health* [*Amer. J. publ. Hlth*] **50**, 14–20, Jan., 1960. 5 figs., 14 refs.

In this paper from the New York State Department of Health, Albany, the observations previously reported by the authors (*Amer. J. publ. Hlth*, 1958, **48**, 1323; *Abstr. Wld Med.*, 1959, **25**, 294) on the effect of residual chlorine in inactivating enteric viruses in water are extended to include combined residual chlorine. In general, two types of observation were made—comparisons of the rates of inactivation of 2 strains of enterovirus at different *p*H levels by one concentration of combined residual chlorine, and estimates of the times of exposure and concentrations of combined residual chlorine required for greater than 99·7% inactivation of a resistant strain. The precautions taken to minimize the chlorine demand, the preparation of solutions and viruses, and the procedures used were, with some exceptions, similar to those described previously.

The results show that the disinfecting action of residual chlorine depends upon hydrogen ion concentration, contact period, and strain of virus. The disinfection is

accomplished more rapidly and with less chlorine when the hydrogen ion concentration is high. The dose of chlorine recommended for the disinfection of sewage, therefore, varies with the *p*H level: at 25° C. and *p*H 7 a concentration of at least 9 parts per million was required for the inactivation of poliovirus with a contact period of 30 minutes, and of 6 p.p.m. with a contact period of one hour; 0·5 p.p.m. necessitated a contact period of more than 7 hours. A decrease in hydrogen ion concentration decreased the rate of inactivation. Differences in resistance to chlorine were found among different strains of virus; the inactivation of a progeny line which survived chlorination was similar to that of the parent line.

The dose of combined chlorine officially recommended for sewage disinfection in many parts of the U.S. (0·5 p.p.m. for 15 minutes) did not inactivate the viruses studied. The data obtained in the present investigation suggest that a longer contact period with small amounts of chlorine may be more effective in destroying resistant strains of viruses than an increased concentration. An alternative to intensified chlorination might be to add a second type of disinfection, such as heat, ionizing radiation, or ultraviolet radiation, to which strains resistant to chlorine may be sensitive.

R. G. Meyer

803. **Cumulative Testing Experience with Consecutive Lots of Oral Poliomyelitis Vaccine**

V. J. Cabasso, G. A. Jervis, A. W. Moyer, M. Roca-Garcia, E. V. Orsi, and H. R. Cox. *British Medical Journal* [*Brit. med. J.*] **1**, 373–387, Feb. 6, 1960. 3 figs., 15 refs.

Brief histories of the three type strains of Lederle attenuated polioviruses have been presented, and production and testing data pertaining to 31 lots of experimental oral vaccine have been described. In all, 113 litres of Type I vaccine, 120 of Type II, and 143 of Type III were prepared and completely tested, yielding quantities sufficient for 4½, 2½, and 4½ million human immunizations, respectively. Only an occasional bacterial contaminant, and no C.N.S., herpes, simian, measles, or B virus was encountered. The presence of tubercle bacilli was also excluded from all vaccine lots, both by guinea-pig inoculation and in culture media.

Intracerebral monkey inoculations of these vaccines produced over-all paralytic rates of 1·5% for Type I, 3·9% for Type II, and 1·2% for Type III. Histopathological changes following inoculation by this route were virtually absent with Type I and Type III vaccine lots. Though early batches of Type II were associated with some neuronal loss, more recent lots have produced almost none. Despite the somewhat greater activity of some Type II vaccines when inoculated intracerebrally, in monkeys inoculated intraspinally activity of lots of all three types was comparable, producing similar over-all paralytic rates. Paralysis induced by this route of inoculation was usually non-progressive and limited to one or both lower limbs, and only an occasional animal died within the 21-day observation period. Histopathological lesions were observed in most of the animals which were inoculated intraspinally, whether or not they were paralysed.

Each of the three Lederle strains of virus has been fed to approximately 500,000 persons in several trials in the U.S.A. and Central and South America. In completed trials comprising 65,429 individuals, or 12% of the total fed, estimated homotypic negatives amounted to 13,959 or 21·3% for Type I, 7,208 or 11% for Type II, and 14,072 or 22% for Type III. In addition there were, among the 65,429 persons surveyed serologically, an estimated 2,750 triple negatives. In not a single instance was a proved case of paralysis or disease attributed to the vaccine.

The intraspinal test has been discussed with regard to its reproducibility and its significance in relation to safety of the vaccine virus for man. The more consistent and more readily carried out intracerebral monkey inoculation has been proposed as the basis for criteria of residual monkey virulence to be used for release of oral vaccine.

Efforts to improve Lederle vaccine strains in every possible way are continuing. Meanwhile the utility of the present strains, in view of the obvious need for a better solution to the problem of immunization against paralytic poliomyelitis, has been demonstrated by the mounting evidence of their effectiveness and safety and the absence of significant undesirable reactions.—[Authors' summary.]

804. **Transmission of Hospital Staphylococci among Newborn Infants. II. Colonization of the Skin and Mucous Membranes of the Infants**

V. Hurst. *Pediatrics* [*Pediatrics*] **25**, 204–214, Feb., 1960. 2 figs., 30 refs.

The rate and sequence in which various body areas of the newborn infant acquire coagulase-positive staphylococci was studied in two hospitals at a time when nursery infections were not occurring. The infants became colonized rapidly on numerous body surfaces in one nursery, and more slowly and less extensively in the other. Skin and rectal cultures usually became positive before those from the nose, throat, and eye. The groin and axilla of infants in one nursery tended to become colonized before the umbilical cord; in the other nursery, colonization of the umbilical cord often preceded that of the groin or the axilla. Different body sites of an individual infant often became colonized with different strains of staphylococci, as determined by phage typing, and two strains sometimes were detected in a single site.

The carrier state of the newborn infant can be assessed accurately only by culturing many body sites and by phage typing many colonies. Cultures of skin, rectum, and umbilical cord are likely to be more informative than nasal cultures, because the nose is often the last site to become colonized. The culture procedure which is most likely to portray the carrier state may have to be determined independently for each hospital nursery to be studied.

It may be difficult to prevent acquisition of hospital strains by applying bacteriostatic substances to the umbilical cord stump or portions of the skin because of the extent to which staphylococci multiply upon the skin, mucous membranes, and perhaps within the intestinal tract.—[Author's summary.]

Industrial Medicine

805. **The Incorporation of Radioactive Methionine-^{35}S in the Proteins of Organs during Acute and Chronic Cadmium Poisoning.** (Включение радиоактивного метионина S^{35} в белки органов при остром и хроническом воздействии окиси кадмия)
R. S. Vorob'eva. *Гигиена и Санитария* [*Gig. i Sanit.*] **25**, 23–26, Feb., 1960. 2 figs., 10 refs.

The effects of acute and chronic cadmium poisoning on protein metabolism were studied by experiments in which the amount of the amino-acid methionine, labelled with radioactive sulphur (^{35}S), which was incorporated into the proteins of various organs and tissues was measured in two series of white rats. In the first series (acute poisoning) a suspension of cadmium oxide in physiological saline was injected intratracheally in a dose of 0·25 mg. per 100 g. body weight, while the second series (chronic poisoning) were made to inhale an aerosol of cadmium in a concentration of 0·0015 to 0·0020 mg. per litre of air for 2 hours every other day for 4 months. At the end of the chronic poisoning and 24 hours after the acute poisoning the labelled methionine was injected, the animals being then killed by decapitation at various intervals after the poisoning, the proteins extracted from the liver, kidney, spleen, lungs, brain, muscles, and whole blood, and the relative radioactivity in the proteins estimated.

The results showed that the rate of incorporation of methionine in the proteins was higher in acute cadmium poisoning and lower in chronic cadmium poisoning than in the control animals. In the animals suffering from chronic cadmium poisoning in the doses given the slowing of the rate of incorporation of the amino-acid was observed long before the appearance of morphological changes in the tissues. *Basil Haigh*

806. **The Effect of Chronic Poisoning with Carbon Tetrachloride and Dichloroethane on the Immunobiological Reactivity of Rabbits.** (Роль факторов внешней производственной среды в иммунобиологической реактивности)
V. K. Navrockij. *Гигиена Труда и Профессиональные Заболевания* [*Gig. Truda prof. Zabolev.*] **4**, 28–32, Jan., 1960.

In this investigation of the effect of industrial poisons on the immunological reactions of animals chronic poisoning was produced in rabbits by means of inhalations of carbon tetrachloride (CCl_4) (4 mg. per litre of air) or dichloroethane (2 mg. per litre) for 2 hours daily. These rabbits, together with control animals not exposed to the poisons, were immunized with typhoid vaccine in 3 doses containing respectively $1{\cdot}5\times10^9$, $0{\cdot}8\times10^9$, and $0{\cdot}8\times10^9$ bacterial cells and the following determinations then carried out: agglutinin titre, complement titre, serum protein level, and blood acetylcholine and cholinesterase levels, as well as morphological examination of the blood and liver (lipids), these determinations being repeated daily for 10 days.

They showed that there was depression of agglutinin formation, which was much more pronounced after dichloroethane than after CCl_4. No significant change took place in the complement titre after poisoning with either compound, nor were there any marked changes in the serum protein pattern. There was, however, a considerable increase in the acetylcholine level and the cholinesterase activity of the blood. No significant changes were found in the erythrocyte count and haemoglobin concentration, but considerable leucocytosis took place, especially after poisoning with CCl_4; such a leucocytosis is frequently observed in the initial stages of poisoning by a number of different substances.

The author concludes that poisons of the chlorinated aliphatic hydrocarbon group cause depression of immunobiological reactivity, and that dichloroethane acts more strongly than carbon tetrachloride in this direction. *Basil Haigh*

807. **Dyspepsia Due to Inhalation of Carbon Tetrachloride Vapour**
G. Kazantzis and R. R. Bomford. *Lancet* [*Lancet*] **1**, 360–362, Feb. 13, 1960. 5 refs.

A male patient aged 34 years attended Poplar Hospital, London, complaining of anorexia, nausea, and occasional vomiting, with a feeling of abdominal discomfort which did not amount to pain. The symptoms had appeared intermittently for about 2 years, and on the present occasion the patient had experienced them for about 2 months, during which time he had felt unusually depressed and irritable; clinical examination revealed no abnormal signs. An unusual feature in the history was that the dyspepsia was better at the week-ends and built up during the week. This led to inquiries about the patient's occupation and it was then found that he was exposed to the vapour of carbon tetrachloride and that other workers had developed similar symptoms. A visit to the factory showed that the workers were employed in a workshop in which the windows were kept closed and in which there was no mechanical ventilation; the room was heated by indirect gas convectors; no atmospheric contamination could be detected on entering the room, but carbon tetrachloride could be smelled in the immediate environment where it was used. The work carried out consisted in the processing of raw quartz in the manufacture of crystals for electronic equipment; the carbon tetrachloride was used for cleaning the crystals, and an ultrasonic vibration of about 40,000 c.p.s. was passed through the beakers of carbon tetrachloride to facilitate the cleaning. The concentration of carbon tetrachloride to which the workers were exposed was approximately 45 to 100 parts per million before covering the beakers and 0 to 60 parts per million after cover-

ing them. Clinical examination of 16 of the 17 workers, performed 5 days after precautions had been taken to reduce further exposure, showed no abnormal physical signs: the fundi and visual fields were normal and examination of the urine revealed no abnormalities. In a study of workers subjected to prolonged exposure to carbon tetrachloride Stewart and Witts (*Brit. J. industr. Med.*, 1944, **1**, 11) found a high incidence of gastro-intestinal upset and mental hebetude, the symptoms reported being similar to those found in the present series with the difference that diarrhoea was a prominent feature. The present authors emphasize that although it is well known that narcosis and damage to the liver and kidneys may be caused by exposure to high concentrations of carbon tetrachloride, it is not so well known that exposure to lower concentrations may cause other and less serious effects. *R. G. Meyer*

808. **The Aliphatic Acids and Their Esters: Toxicity and Potential Dangers.** [Review Article]
W. F. VON OETTINGEN. *A.M.A. Archives of Industrial Health* [*A.M.A. Arch. industr. Hlth*] **21**, 404–423, May, 1960. 5 figs., bibliography.

OCCUPATIONAL DISEASES

809. **Observations on a Labyrinthine Syndrome Appearing Suddenly in Telephonists.** (Observations sur un syndrome labyrinthique apparu subitement chez des téléphonistes)
G. P. ALIVISATOS, C. E. ELIAKIS, and A. E. PONTIKAKIS. *Archives des maladies professionnelles, de médecine du travail et de sécurité sociale* [*Arch. Mal. prof.*] **21**, 33–40, Jan.–Feb., 1960. 5 refs.

Writing from the University of Athens the authors record their observations on 41 telephone operators employed at the Athens Central Telephone Exchange who, 2 to 3 hours after starting work in July, August, and September, 1955, reported with symptoms of headache, vertigo, nausea, pallor, trembling of the legs, instability on walking, and muscular and intellectual fatigue. The first three symptoms were present in approximately 78% of the cases. Of these 41 workers, of whom 36 were aged between 18 and 34, 33 were subjected to a detailed vestibular and general examination, and the environmental conditions of work, such as ventilation, temperature, humidity, carbon monoxide content of air, and duration of duty were investigated; a group of 12 similarly employed telephonists with no such symptoms served as a control.

The findings were as follows: (1) Two-thirds of the 33 workers examined showed labyrinthine hypersensitivity (this may have been present at all times). (2) All the subjects stated that the reactions provoked by the labyrinthine tests were similar to the symptoms experienced at work. (3) None of the control group had a hypersensitive labyrinth. At first the symptoms were regarded as functional in origin, but the results of the detailed examination convinced the authors that they were labyrinthine. After the environmental conditions had been improved and the number of telephone calls dealt with by each operator had been reduced no further cases were reported between 1955 and 1958. It is concluded that mental fatigue is the principal cause of the symptoms observed and that this fatigue was related not only to the number of telephone calls dealt with, but also to the necessity of keeping check on the duration of the calls. *E. D. Dalziel Dickson*

810. **Harmlessness of Coal Dust to Cellular Protoplasm. Demonstration by Electron Microscopy.** (Innocuité des poussières de houille pour le protoplasma cellulaire. Démonstration par microscopie électronique)
A. POLICARD, A. COLLET, and S. PREGERMAIN. *Presse médicale* [*Presse méd.*] **67**, 2263–2265, Dec. 25, 1959. 3 figs., 12 refs.

It has been shown by microcinematography that phagocytes move normally when charged with coal particles, but that their movement is impaired when they contain silica particles. The difference between the effect of these two types of particle on cells is further confirmed in this paper from the Centre d'Études et Recherches des Charbonnages de France, Paris and Verneuil-en-Halatte (Oise). Electron microphotographs were taken of phagocytes from the lungs of rats given a mixture of anthracite and silica particles 7 days previously by the intra-tracheal route. A special technique permitted sections 0·04 μ thick to be cut. There was no apparent modification in the structure of the cytoplasm in the neighbourhood of the intracellular coal particles. Around the silica particles on the other hand the cytoplasm appeared modified, and the authors suggest that the proteins are denatured by the silica.
C. M. Fletcher

811. **The Functional State of the Adrenal Cortex in the Early Stages of Experimental Silicosis.** (О функциональном состоянии коры надпочечников на ранних стадиях экспериментального силикоза)
N. K. DAVTJAN. *Проблемы Эндокринологии и Гормонотерапии* [*Probl. Endokr. Gormonoter.*] **6**, 26–32, Jan.–Feb., 1960. 26 refs.

Depression of adrenocortical activity in patients with advanced silicosis has been reported by several observers. The present author has now performed experiments on white rats to determine the effect of silicosis in the early stages on adrenocortical function, the silicotic lesions being induced by the intratracheal injection of 0·4 ml. of colloidal silicic acid solution, prepared by adding hydrochloric acid to sodium silicate and dialysing. At intervals of 1, 2, 7, 15, and 30 days after such injection 5 of the animals were killed and the ascorbic acid content of the adrenal glands assayed, eosinophil and lymphocyte counts made on the peripheral blood, and Thorn's test performed. At the same time 15 untreated healthy rats were similarly examined and served as controls.

The ascorbic acid content of the adrenal glands was found to rise in each successive group killed up to 15 days, after which there was a fall in content. The eosinophil and lymphocyte counts fell steadily after the 2nd day, but still exceeded those in the normal controls after

30 days. Thorn's test was progressively weaker in successive groups and in all cases weaker than in the control group. The author suggests that the increase in adrenal ascorbic acid content may be explained either by increased biosynthesis of the substance in the glands or by lowered synthesis of hormones. He tends to lean to the latter explanation and on this view all the results point to a depression of adrenocortical function from the earliest stages of experimental silicosis.

L. Firman-Edwards

812. **Comparative Study of Cardiovascular and Respiratory Involvement in Pulmonary Asbestosis.** (Analisi comparata della compromissione cardiovascolare e respiratoria nell'asbestosi polmonare)

G. SCANSETTI and G. F. RUBINO. *Minerva medica* [*Minerva med. (Torino)*] **51**, 8–17, Jan. 6, 1960. 6 figs., 21 refs.

Writing from the General Medical Clinic of the University of Turin the authors point out that four stages can be recognized radiologically in the development of pulmonary asbestosis: (1) fine reticulation extending from the hila to the lower fields without any change in the heart shadow; (2) slight fibrosis, accentuated hilar shadows, appearance of fine reticulation in the mid-fields giving a "ground-glass" appearance, cardiac outline not so distinct as in Stage 1; (3) diffuse fibrosis with irregular opacities in the lower fields and extending right up to the apices, marked blurring of the heart shadow; (4) this is only rarely seen because the patient usually dies before it occurs; there is grave fibrosis, retraction of the pulmonary fields, complete occlusion of the cardiac outline, numerous opacities in the lower lung fields, and marked transparency in the upper lung fields. The special respiratory changes consist in a general reduction in lung capacity and also in its individual components, while the early signs of respiratory insufficiency are due to changes in the processes of diffusion across the capillary-alveolar membrane. However, what effects, if any, these have on the heart remains undetermined.

An examination of the x-ray picture and investigation of respiratory and cardiovascular function were carried out on 34 patients, 21 male and 13 female, aged 33 to 72 years who were, or had been, working with asbestos for periods ranging from 5 to 35 years, the duration of their symptoms ranging from 1 to 17 years. [In 9 cases the duration is not stated.] Only one man had worked in an asbestos mine, the rest having been employed in processing the fibres. In 27 cases the patient complained of dyspnoea on exertion, often accompanied by cough or a "heavy" feeling. Radiologically, 8 were in the 1st, 12 in the 2nd, 13 in the 3rd, and one in the 4th stage. An electrocardiogram with all the usual leads was recorded from all patients, and in 13 cases cardiac capacity was tested by the sphygmographic method of Wezler and Böger. The QRS axis was not usually altered with the progress of the disease, but 8 patients in the 3rd stage showed some effects on the left ventricle. Cardiac capacity was reduced to the lowest normal limits or even below these, but cor pulmonale was not found in any of the patients examined. There was a uniform reduction in the vital capacity from stage to stage and diminution in the total lung capacity was especially marked in the 2nd and 3rd stages. In its evolution asbestosis causes, in addition to a reduction in the parenchyma available for gaseous exchange, a special rigidity of the lung, while the functional changes are more marked than the radiological, asbestosis differing in this respect from silicosis. There are indications that there is also an emphysematous component.

[In view of the alleged association between asbestosis and cancer of the lung it is greatly to be regretted that the figures given in the text and in Table 1 do not agree. In the text it is stated that 4 patients had associated pulmonary tuberculosis and 2 lung cancer, while the table gives 1 for tuberculosis and 4 for cancer.]

W. K. Dunscombe

813. **Bronchial Changes in Silicosis: a Bronchoscopic, Bronchographic, and Bacteriological Study.** (Le alterazioni bronchiali nella silicosi: studio broncoscopico, broncografico e batteriologico)

G. MERLO, A. MONTEVERDE, and M. CORNAGLIA. *Minerva medica* [*Minerva med. (Torino)*] **51**, 18–32, Jan. 6, 1960. 19 figs., 24 refs.

The authors point out that it is only recently that the changes in the bronchi in silicosis have been studied in respect of their ability to cause serious respiratory incapacity independently of the parenchymal changes. They emphasize that, clinically, the silicotic is a bronchitic, whereas the question of compensation is nearly always settled on the basis of a standard radiograph, sometimes with tomograms, without consideration of the bronchial picture. On the other hand bronchoscopy and bronchography show that serious bronchial lesions with resulting incapacity may be present without marked radiological changes.

The authors then report on 88 cases of silicosis in whom bronchoscopy and bronchography, with aspiration of bronchial secretion, culture of the contained organisms, and in some cases biopsy of the bronchial mucosa, were carried out. The patients fell into the following groups: (1) 20 with micronodulation; (2) 27 with nodulation; (3) 22 with confluent or massive lesions; and (4) 19 with silicosis in various stages associated with pulmonary tuberculosis. Few had been exposed to risk for less than 10 years. In 84 cases bronchoscopy or bronchography was performed, and all underwent standard radiography and tomography and certain laboratory tests were performed to try and estimate the stage of disease. For bronchography, propyliodone barium gave high opacity and very little cough and was eliminated in 48 hours.

In Group 1 13 patients showed some stenosis; bacteria were scarce or absent in 15 and one had egg-shell calcification. In Group 2 all 27 patients showed reduction in the lumen of the bronchi of an extrinsic nature and spasm of the large bronchi was seen frequently; 13 had stenosis and 2 occlusion, egg-shell calcification occurred in 2, and 3 had the middle-lobe syndrome; bronchiectasis was present in 2, and one patient had a cavity which was ascribed to liquefaction of the fibrosclerotic material and not to tuberculosis. In Group 3 atrophy of the bronchial mucosa was seen in 16 cases

and stenosis in 13; in 6 the lymph nodes were very much enlarged, and signs of emphysema were evident, with bronchiectasis especially of the upper lobe and the apico-dorsal section of the lower lobe. In Group 4 17 out of 19 samples of secretion taken at bronchoscopy were positive for tubercle bacilli; in one case after bronchoscopy and bronchography with biopsy a diagnosis of carcinoma was made which had to be changed after necropsy to silico-tuberculosis. Special mention is made of the difficulty of detecting atelectasis in Groups 3 and 4. It is emphasized that bronchography demonstrates at all stages the effects of compression from hypertrophied lymph nodes, the middle-lobe bronchus being most often affected. Biopsy of the mucosa in Stages 1 and 2 showed hyperplasia and congestion suggesting recent bronchitis which, with the passage of time, tends to go on to atrophy.

The authors conclude that bronchoscopy and bronchography are valuable aids in estimating the functional respiratory capacity in silicosis.

[There are some excellent bronchograms and coloured bronchoscopic illustrations. See also the paper by Grazioli *et al.*, in the same issue, on the use of this technique in byssinosis (Abstract 814).]

W. K. Dunscombe

814. **Clinical Study of 8 Cases of Byssinosis, with Particular Reference to the Bronchographic and Bronchoscopic Appearances of the Disease.** (Studio clinico di 8 casi di bissinosi con particolare riguardo agli aspetti broncografici e broncoscopici della malattia)
C. GRAZIOLI, G. MERLO, and A. MONTEVERDE. *Minerva medica* [*Minerva med. (Torino)*] **51**, 41–52, Jan. 6, 1960. 15 figs., 21 refs.

After a preliminary discussion of byssinosis, cotton worker's asthma, and weaver's cough in which they point out that in their late stages the clinical signs and symptoms of all three are practically identical, the authors report their findings in 8 patients carefully selected from a larger number of cotton workers with evidence of some bronchial condition. The patients were examined by a battery of laboratory tests, tests of respiratory capacity, radiography (including tomography), skin tests for allergy, and more particularly by bronchoscopy and bronchography with examination of the sputum and biopsy of the mucosa. The ages of the patients ranged from 26 to 45 years, 4 were males and 4 females, and 2 worked in the preparing, 2 in the carding, and 4 in the weaving sections of cotton mills. The youngest, a woman of 26, had worked as a weaver for 12 years. The authors draw attention to the relatively young ages of the patients and point out that symptoms appeared earlier among the weavers. Five initially had the typical " Monday fever ", though the course of the disease was similar in all 8 and was considered to be true byssinosis.

The classic signs of chronic bronchitis with asthma and emphysema were found, but in none was the right heart affected. All had eosinophilia, suggesting an allergic origin. Nothing very informative was found on bacteriological examination of the sputum even after bronchoscopy, nor did plain radiography and tomography show anything that could specifically be ascribed to byssinosis. In 7 cases bronchoscopy showed a diffuse hypertrophic bronchitis affecting especially the middle-lobe bronchus, while in all there was evidence of stenosis of the segmentary bronchi which could be ameliorated temporarily by adrenaline. On biopsy the most significant change in the mucosa was the global hyperplasia. Bronchography showed in all cases diffuse and often grave changes in the bronchi with a brusque termination of the segmentary bronchi, giving a " lopped-tree " appearance, and evidence of compression by hypertrophied lymph nodes. There were signs of emphysema affecting particularly the lower lobes on both sides, with small opaque spots due to the confluence of numerous alveoli causing a practically pathognomonic change in the broncho-alveolar outlines. There was a marked reduction in the vital capacity and inspiratory volume. All the patients gave definitely positive reactions to sensitivity tests with extracts of cotton dust, indicating the elements responsible for the initial disease. Desensitization was carried out in 5 cases and resulted in diminution of the asthmatic attack, though symptoms of respiratory insufficiency persisted.

The authors conclude that although the number of patients examined was small, the tests showed only a chronic asthmatic bronchitis, with nothing really specific for byssinosis. However, the bronchograms and respiratory tests showed how grave were the effects of the disease on the respiratory system. They point out that so far they are not aware of any other cases of byssinosis in which bronchoscopy and bronchography have been performed, and finally suggest that in Italy, as in Britain, byssinosis should rank for compensation. [There are some excellent bronchograms.] *W. K. Dunscombe*

815. **A Clinical and Environmental Study of Byssinosis in the Lancashire Cotton Industry**
S. A. ROACH and R. S. F. SCHILLING. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **17**, 1–9, Jan., 1960. 2 figs., 16 refs.

This paper from the London School of Hygiene and Tropical Medicine reports a study of 189 male workers and 780 female workers employed in three coarse- and two fine-cotton mills in Lancashire, these numbers representing 98% of the male and 96% of the female employees. The clinical symptom of chest tightness on Monday morning is the specific response to inhaling cotton dust. Among workers in the card-rooms of the coarse-cotton mills 63% of the men and 48% of the women had this symptom; among those in the card-rooms of the fine-cotton mills on the other hand the corresponding incidences were only 7 and 6% respectively. The over-all incidence in the spinning rooms was much lower (2%). An instrument based on the hexhlet described by Wright (*Brit. J. industr. Med.*, 1954, **11**, 284) was used to measure the dust concentration to which the workers were exposed at 505 different working places. The mean dust concentrations in the different rooms ranged from 90 mg. per 100 c. metre in one section of the card-room in a fine-cotton mill to 440 mg. per 100 c.m. in one of the card-rooms of the coarse-cotton spinning mills, and the prevalence of

byssinosis was found to be closely related to the over-all dustiness.

The disease seemed to be related to the protein present in the dust and not to the size of the dust particles. It was shown that dust particles of less than 7 μ in diameter were less important than the larger particles. The explanation of this may be that much more of the dust is in the medium and coarse size range than in the fine range. In the card-rooms of the coarse-cotton mills it was found that in every 100 mg. of dust there was about 6 mg. of medium protein and 1·5 mg. of fine protein. Thus the amount of the sensitizing agent in the fine dust is probably less than in dust in the medium-sized range. Furthermore, the sensation of tightness in the chest may originate in the respiratory tract above the level of the terminal bronchioles, that is, where most of the medium-sized particles are deposited. It is possible, however, that fine dust may cause damage to the terminal bronchioles or alveoli without necessarily causing the sensation of chest tightness. Bacteria and moulds are present in relatively high concentrations in the atmosphere of cotton-mill card-rooms and have also been considered as possible causes of byssinosis. However, Tuffnell has shown that when 3 men with disabling byssinosis were exposed to an inert dust carrying *Bacillus pumilus* and *Aspergillus niger*, the most common species of bacteria and fungi found in cotton mills, they developed no clinical symptoms and showed no reduction in ventilatory capacity.

The amount of dust in the air of a cotton mill seems to depend on the quality of the cotton being processed, the weight of cotton spun per week, and the amount of ventilation in the rooms. The more dirt, " trash ", and short fibre there is in the cotton, the greater is the concentration of airborne dust. It is known that the Shirley pressure-point system, which is a local exhaust ventilation system applied to the dusty points of a carding engine, substantially reduces the dust concentration in the card-rooms with benefit to the workers. Nevertheless it seems that neither this system nor those systems which increase general ventilation can reduce the dust concentration to safe levels in the most dusty card-rooms. The authors suggest that a realistic target level of dustiness in these rooms which would be accepted and could be achieved in practice is a maximum of 250 mg. per 100 c.m. Even this is not a safe level, although it would undoubtedly reduce the incidence of the disease. For a cotton mill to be reasonably safe the concentration would have to be less than 100 mg. per 100 c.m.

Kenneth M. A. Perry

816. **A Study of Heat Stress in Extremely Hot Environments, and the Infra-red Reflectance of Some Potential Shielding Materials**

C. E. Lewis, R. F. Scherberger, and F. A. Miller. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **17**, 52–59, Jan., 1960. 6 figs., 8 refs.

From the Eastman Kodak Laboratory of Industrial Medicine, Rochester, New York, the authors describe an attempt to evaluate the effects of exposure to industrial heat in three very hot environments, designated A, B, and C, at a glass works. Areas A and B were in two enclosed paper-making machines and Area C was in a drying alley. The heat-stress index (H.S.I.) of Belding and Hatch, which is arrived at by utilizing the wet-bulb, dry-bulb, and globe temperatures, the air velocity of the environment, and the metabolic heat load produced by the activity of the subject, was 524 in Area A, 397 in Area B, and 395 in Area C. An index of 100 describes the maximum heat stress to which an acclimatized healthy young male can be subjected for 8 hours without showing adverse physiological changes. However, calculations of permissible exposure within an area having a certain heat stress index is ultimately based upon the original definition of a safe tolerance limit, which has been defined as the time required to raise the pulse rate by 40 to 45 beats per minute and the body temperature 2° F. (1·1° C.).

The study was performed on 3 healthy men aged between 30 and 40 and weighing from 79 to 82 kg. who were unacclimatized to unusual heat; during the tests they wore light cotton clothing In Area A, with an H.S.I. of 524 which, according to the method of Belding and Hatch, would allow a maximum exposure of only 7·6 minutes, the 3 individuals showed rises in the pulse rate of 26, 30, and 22 beats per minute respectively and an oral temperature increase of 0·9° F. (0·5° C.) after 20 minutes' exposure In Area B (H.S.I. 397 and calculated maximum exposure time 8·4 minutes) the pulse rates rose by 40, 62, and 48 beats a minute and the temperature by 1·7° F. (0·95° C.) after 22 minutes. In Area C (H.S.I. 395 and maximum exposure time 5·3 minutes) the pulse rates rose by 34, 28, and 28 beats a minute and the temperature by 1·7° to 2·1° F. (0·95 to 1·2° C.) in 20 minutes. These figures show that the maximum exposure times obtained by the Belding and Hatch method err on the safe side by a considerable margin, being only about one-third of those allowed by physiological measurements. It is noted that the latter are comparable with those recommended by the American Society of Heating and Ventilating Engineers on the basis of heat stress tolerance curves.

Much of the data used by Belding and Hatch in deriving the H.S.I. were based on tests on nude subjects. Their assumption that the wearing of light clothing would have little influence upon the heat exchange of the body by conduction and convection is evidently valid in environments in which the H.S.I. is below 100. However, when the thermal gradient between skin and environmental temperature is markedly increased the wearing of even light clothing appears to have a significant effect upon the index. One of the advantages of the Belding and Hatch index is that it yields values of the individual components of heat stress, that is, heat gains due to radiation, convection, and conduction, and includes an estimate of evaporative heat losses. In Areas A and B about half the heat burden incident upon the test subjects was due to radiation. Thus to cool a worker in such an area it is necessary to reduce the heat gain due to radiation by reducing infra-red radiation at its source, or by reflecting it from the individual by means of shields. The intelligent use of shielding as a method of protecting workers from radiant heat requires a

knowledge of the infra-red reflectance curves of common industrial materials, and 19 such curves are included in this paper. *Kenneth M. A. Perry*

817. **The Pathogenesis of Chrome Eczema.** (De pathogenese van het chroomeczema)
J. W. H. MALI. *Archives belges de dermatologie et de syphiligraphie* [*Arch. belges Derm.*] **15**, 390–412, Dec., 1959 [received Feb., 1960]. 15 figs., 5 refs.

An investigation of the pathogenesis of chromium eczema was undertaken at the University of Nijmegen, Netherlands, by a combination of histological, allergic, electrochemical, and biochemical tests and experiments on animals and human volunteers. In histological investigations of biopsy specimens of skin taken 6 and 12 hours after carrying out a patch test with dichromate the first manifestations of inflammation were localized around the sweat glands, the typical dichromate reaction being therefore a periporitis. Moreover, in patch tests carried out on persons hypersensitive to dichromate it was found that the reaction was more intense if the skin was previously treated with pilocarpine in order to increase the activity of the sweat glands, whereas in areas previously treated with formalin the result was usually negative. The intensity of the reaction to dichromate was found to be proportional to the product of the concentration of dichromate and the time of application. It would appear therefore that dichromate passes through the sweat glands by a process of simple diffusion. Tests with dichromate containing radioactive chromium showed that the amount of dichromate passing through the intact epidermis into the dermis was very small in both normal and hypersensitive persons. These findings support the author's hypothesis that chromium eczema is caused by chromium salts passing through the epidermis via the sweat glands, where they cause no damage, and then passing to the dermis, where they cause inflammation which involves the epidermis only secondarily.

The reactions which chromium in two different valency states enters into with the skin were studied with potassium dichromate (hexavalent) and basic chromium sulphate (trivalent). Iontophoresis experiments carried out *in vitro* with membranes of epidermis showed that dichromate was drawn through the sweat glands, but that it was impossible to draw basic chromium sulphate through the epidermis owing to its precipitation in the top layers of the epidermis. These findings were confirmed by determinations of the membrane potentials of membranes of skin and dermis, which also indicated that dichromate was bound, and possibly reduced, in the dermis.

The histology of the inflammatory reaction was studied in guinea-pigs sensitized with potassium dichromate, which were subjected to patch tests followed after 3 weeks by the intradermal injection of dichromate. The intradermal tests resulted in an inflammatory reaction of the same type as the Arthus phenomenon. Biopsies of the skin of normal animals taken 72 hours after the application of dichromate and basic chromium sulphate showed no abnormality. In the sensitized skin an inflammatory reaction occurred with both substances which passed into acanthosis 72 hours after the application of basic chromium sulphate, but had hardly started to resolve in this time after application of dichromate. In intradermal tests on 10 patients and 10 control subjects with various fractions of the dermis freed from unbound chromium by dialysis no reactions were observed, but a small papule was observed in one-half of the cases when dichromate was added in high dilution (10^{-7} to 10^{-8}) and after 48 hours a typical dichromate reaction was observed. Dichromate alone produced a reaction only when injected in quantities 1,000 to 10,000 times as great.

It is suggested that the ground substance of the skin has a non-specific effect on the reaction, and a search for an antigenic complex which may arise from the action of dichromate on the skin is being made.

Anne Tothill

818. **Physiological Changes during Work at Control Desks in Operators on the Moscow Underground Railway.** (Физиологические сдвиги в процессе работы за пультом управления у дежурных и операторов Московского метрополитена)
A. I. KIKOLOV. *Гигиена Труда и Профессиональные Заболевания* [*Gig. Truda prof. Zabolev.*] **4**, 20–26, Feb., 1960. 5 figs., 7 refs.

Operators at control desks serving sectors of the track of the Moscow underground railway system are responsible for the movements of trains in their particular sector. The work entails observing illuminated charts, watching several changing processes at the same time which involves shifting the attention rapidly from one to another, making rapid decisions, and rapidly carrying them out. This work thus calls for high responsibility and requires great concentration and its effect on the operators was therefore investigated by means of a series of physiological tests. Photochronometry showed that for 87·9% of their shift time the operators were actually working, for 10·3% they were occupied in preparation, and only for 1·8% could they rest. The functional mobility of the visual analyser was measured by means of an electronic stimulator. The critical frequency of stimulation was found to be increased at the mid-point of the shift and diminished towards the end. Investigation of higher nervous activity showed an increased latent period of formation of conditioned reflexes after the shift. The blood sugar level and arterial blood pressure were both increased towards the middle of the shift.

The author concludes that under these conditions of almost continuous exacting work under great strain fatigue is inevitable and is usually marked after 4 hours. He recommends that there be a break of one hour for rest in the middle of the shift, and that this hour be deducted from the length of the working day.

Basil Haigh

819. **Occupational Health Studies of the Shell-molding Process**
G. E. TUBICH, I. H. DAVIS, and B. D. BLOOMFIELD. *A.M.A. Archives of Industrial Health* [*A.M.A. Arch. industr. Hlth*] **21**, 424–444, May, 1960. 13 figs., 10 refs.

Radiology

820. **Marrow Transplantation after Radiation: an Experimental Approach to the Immunological Complications**

K. A. PORTER. *Clinical Radiology* [*Clin. Radiol.*] **11**, 22–32, Jan., 1960. 17 figs., 31 refs.

The author describes two animal experiments performed at St. Mary's Hospital Medical School, London, which were undertaken to ascertain the cause of the immunological complications which follow the transplantation of homologous bone marrow after lethal doses of radiation and which are the cause of the high delayed mortality from the condition known as " secondary disease ". The animals used were young adult rabbits, all males, which were not inbred in the genetic sense, and they were given whole-body x-irradiation to a total dose of 1,600 r. in three exposures 24 hours apart, equivalent to an $L.D._{100}$ at 30 days; all also received an antibiotic for 2 weeks following irradiation. Marrow and lymph-node suspensions were taken from female rabbits of the same strain and total and differential leucocyte counts performed; the phenomenon of radiation-chimaera was confirmed by finding female sex chromatin in the heterophils.

The first experiment was designed to test the " graft-versus-host " hypothesis, that is, that the few stem cells introduced with the marrow produce foreign lymphoid tissue which acts against the host's antigens to produce secondary disease. If this were true the introduction of greater numbers of lymphoid cells might be expected to accelerate the secondary disease. The rabbits were therefore divided into five groups. (1) Non-irradiated rabbits were given lymph-node suspensions only and showed no reaction. The remaining four groups all received whole body x-irradiation and were treated as follows: (2) were given only saline injections after irradiation and served as controls; (3) were given an injection of lymph-node cells alone; (4) received a single intravenous injection of fresh bone marrow from a female rabbit; and (5) received a similar dose of bone marrow together with a suspension of lymph-node cells. The results were that the rabbits in Group 3, treated with lymph-node cells alone, died more quickly than did the controls. Those in Group 5 died more quickly than those in Group 4, that is the addition of lymph-node cells increased the severity of the reactions. In addition the rabbits in Group 5 showed post-mortem evidence of wasting and of diarrhoea similar to that seen in secondary disease; the bone marrow also resembled that seen in secondary disease.

In a second experiment whole-body irradiated rabbits were treated with liver extracts from newborn rabbits and from 20-day foetuses, since it had been shown previously that the proportion of animals dying in the first 3 months from secondary disease was reduced from 35% in those treated with adult bone marrow to 20% in those given newborn-rabbit liver and to zero in those given foetal liver instead of bone marrow. This further study of the length of survival after these different treatments showed that: (1) of the rabbits given adult female bone marrow, 74% were dead at 10 weeks and 84% at 17 weeks; (2) of those given newborn rabbit liver, 70% were dead at 10 weeks, 73·4% at 20 weeks, 80% at 30 weeks, and 83·4% at 35 weeks; and (3) of those receiving foetal hepatic tissue, 44% were dead at 17 weeks, 50% at 20 weeks, and 54% at 25 weeks. In the last group 7 animals developed a mild form of secondary disease, but recovered.

The author concludes that an early hostile immune reaction to host antigens occurs in the foreign lymphoid cells, and that secondary disease is the result of a similar but slower process. He suggests that the reduction in incidence or attenuation of secondary disease after treatment with foetal liver is due to the partial tolerance possessed by maturing foetal cells for host antigens. He concludes with the warning that if this hypothesis should be correct the transfusion of whole blood or leucocytes into heavily irradiated subjects may in fact be harmful.

D. Pearson

RADIODIAGNOSIS

821. **Radiologic Aspects of Stab Wounds of the Chest**

L. C. DOUBLEDAY. *Radiology* [*Radiology*] **74**, 26–33, Jan., 1960. 4 figs., 6 refs.

The value of initial radiographs in cases of stab wounds of the thorax is discussed in this paper from the Columbia–Presbyterian Medical Center and the College of Physicians and Surgeons, New York.

Supraclavicular wounds may appear insignificant, but a chest radiograph may show widening of the superior mediastinal shadows resulting from haemorrhage into the mediastinum. This leads rapidly to compression of the great veins and the atria of the heart. Usually as pressure mounts the mediastinal pleura ruptures and associated haemothorax develops. The diagnosis of haemothorax is based on the finding of a significant separation of the fundus of the stomach from the air-filled base of the lung. In an antero-posterior supine radiograph the blood will be seen to be dispersed over the surface of the lung.

It is estimated that in the case of pericardial wounds 200 ml. of fluid may be present in the pericardial sac without altering the cardiac contour. Chest radiography may therefore not be of help in diagnosis, particularly if a portable apparatus is used. Straightening of the left border of the heart has been noted in cases of acute haemopericardium. Serial radiographs of the

chest are necessary to detect re-accumulation of fluid and delayed pericardial effusion.

The extent of injury caused by penetrating wounds of the lower thoracic region may not be readily apparent, especially if the instrument used was long and thin. Initial chest radiographs may show nothing apart from a pneumothorax. Radiography of the abdomen, however, may reveal a change in the splenic shadow, indicating a haemorrhage into this organ; this alteration in contour may be a late finding so that serial radiographs are necessary. *John H. L. Conway-Hughes*

822. **Chest Roentgenographic Changes in Systemic Lupus Erythematosus**

J. G. BULGRIN, E. L. DUBOIS, and G. JACOBSON. *Radiology* [*Radiology*] **74**, 42–49, Jan., 1960. 3 figs., 15 refs.

In this paper from the University of California School of Medicine and the County Hospital, Los Angeles, the authors describe the radiological appearances of the chest in 207 cases of systemic lupus erythymatosus. In 96 cases no radiological abnormality was found; a considerable number of these cases had been followed up over many years and in 8 of them no intrathoracic involvement was found at necropsy. Pleural changes occurring as an isolated abnormality as well as in combination with cardiac or pulmonary lesions were observed in 69 cases. Effusions were usually small and in almost half the cases they were bilateral. Abnormal cardiac changes were noted in 72 cases. In the main these consisted in non-distinctive enlargement of the heart, usually minimal to moderate in degree; in just under half of the cases they were associated with pleural changes. Pulmonary change was demonstrated in 26 cases; in 5 of these it was due to disease unrelated to the lupus erythymatosus. Pulmonary oedema was present in 5 cases, but 2 of these were terminal. A pneumonic type of consolidation was observed in 13 cases; in 7 it was a rapidly resolving single event, in 4 it was recurrent, and in 2 it was of a non-specific infiltrative type of unknown duration. In the remaining 3 cases there were respectively rapidly progressive, massive terminal pneumonia, long-standing consolidation, and variable, patchy, and nodular recurrent infiltrations.

[The main difference between this and other reported series is the high incidence of cases without abnormality; there appeared to be no explanation for this.]

John H. L. Conway-Hughes

823. **Chronic Bronchitis and Emphysema at Bronchography**

A. K. FREIMANIS and W. MOLNAR. *Radiology* [*Radiology*] **74**, 194–205, Feb., 1960. 18 figs., 39 refs.

The bronchographic features in chronic bronchitis have been studied in 2,000 bronchograms obtained over a 5-year period at the Ohio State University Hospital, Columbus, Ohio. The principal abnormalities detected were as follows. (1) Bronchial spasm producing bronchial narrowing or complete obstruction. (2) Non-filling of smaller branches due to emphysema. (3) Globules of secretion in the bronchi. (4) Bronchial obstruction due to inflammatory changes in the bronchial wall in addition to spasm or mucous block. (5) Patchy alveolization due to different rates of air flow. (6) Bronchiolectasis, producing rounded pools 2 to 6 mm. in diameter. (7) Irregularity and deformity of the bronchial wall in the more severe cases. (8) Atrophy of the bronchial mucosa producing annular areas of slight widening and narrowing. (9) Mucous gland dilatations, sometimes amounting to multiple diverticula, particularly in the trachea and major bronchi. *D. E. Fletcher*

824. **The Roentgenographic Appearance of Eosinophilic Lung (Tropical Eosinophilia)**

F. Y. KHOO and T. J. DANARAJ. *American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine* [*Amer. J. Roentgenol.*] **83**, 251–259, Feb., 1960. 4 figs., 25 refs.

The radiological appearances of eosinophilic lung are described with reference to 550 cases seen at the General Hospital, Singapore. The disease is characterized by chronic cough which may be spasmodic and resemble bronchial asthma. An eosinophilia, usually of more than 5,000 eosinophils per c.mm., establishes the diagnosis. Typically the chest radiograph shows an increase in lung markings and mottling in both lungs. The shadows are usually discrete, soft, and ill-defined and may vary in size up to about 4 mm. in diameter. Of the cases examined, 373 showed increased markings and mottling, while more extensive pneumonic changes were seen in 30; increased lung markings only were demonstrated in 138 and in 9 the radiograph appeared normal.

Treatment with organic arsenic or, better still, with diethylcarbamazine usually results in a cure within a few weeks; in these cases the radiological picture may revert to normal. *A. M. Rackow*

825. **The Diagnosis of Pericardial Effusion with Intracardiac Carbon Dioxide**

J. H. SCATLIFF, A. J. KUMMER, and A. H. JANZEN. *Radiology* [*Radiology*] **73**, 871–883, Dec., 1959. 11 figs., 10 refs.

To differentiate radiologically between an enlarged heart and a pericardial effusion may be difficult. The authors have made use of the fact that in animal experiments carbon dioxide in relatively large amounts has been injected intravenously without danger of pulmonary embolism or other untoward effect.

Carbon dioxide passes into the right auricle and, if the patient is lying on the left side, the bubble collects uppermost against the atrial wall and remains trapped for a minute or more. Radiographs taken postero-anteriorly in the left decubitus position with a horizontal ray show the outline of the gas in the atrial cavity separated from the right lung field by a radio-opaque band which represents the wall of the atrium, the pericardium, and the pleura. In the healthy subject and in the patient with an enlarged heart this band is about 3 mm. in width and even allowing for fat accumulation the shadow should not be more than 5 mm. The presence of pericardial fluid or pericardial thickening causes a widening in this band which is diagnostic. About 50 ml. of carbon dioxide is injected and a serial radiograph changer is

used taking one radiograph per second for several seconds.

The authors, at Yale–New Haven Medical Center, Connecticut, have examined 22 patients by this method and have found it both highly reliable and reasonably free from hazard. The cases illustrated demonstrate the diagnostic value of this examination and the authors discuss certain criteria that may be used to differentiate the presence of pleural fluid from pericardial thickening.

A. M. Rackow

826. **Roentgenography and Biopsy in Mammary Cancer**
S. M. BERGER, H. INGLEBY, and J. GERSHON-COHEN. *Radiology* [*Radiology*] **73**, 891–895, Dec., 1959. 4 figs.

X-ray examination of the breast can achieve a high level of accuracy. With clear-cut findings of a definite benign or malignant lesion, the accuracy is better than 95%. When the x-ray findings are less clear-cut, the diagnosis is less reliable; this is true of approximately 10% of all breast examinations, particularly in adolescents and some young adults. The older the patient, and the larger and fatter the breasts, the easier is the x-ray diagnosis.

Malignant lesions can be uncovered by roentgenography when they are relatively small. In these cases, the incidence of axillary metastases is less than in palpable lesions evident to the patient or the surgeon. In a series of 48 unsuspected or asymptomatic cancers detected by x-ray studies, the incidence of axillary lymph node metastasis was only 13% in contrast to 64% in cases diagnosed at surgery. From a study of 16 cases with delayed operations, it was found that the x-ray examination was positive from 1½ to 4 years before the lesions became evident to the patient or the surgeon.—[Authors' summary.]

827. **The Radiological Diagnosis of Regional Enteritis.** (Zur Röntgendiagnostik der Enteritis regionalis)
H. SCHLOTTER. *Fortschritte auf dem Gebiete der Röntgenstrahlen und der Nuklearmedizin* [*Fortschr. Röntgenstr.*] **92**, 1–19, Jan., 1960. 15 figs., 31 refs.

After describing briefly the pathological changes and clinical manifestations and course of regional enteritis the author reports observations on 6 cases of his own, some of which were followed up for several years, with particular reference to the variations in the radiological appearances. He emphasizes the need for serial x-ray examinations in the assessment of the course of the disease and the evaluation of the treatment.

[As always in this journal, x-ray films and photographs of specimens are beautifully reproduced.]

Denys Jennings

828. **Ward Barium Meal Examination in Acute Gastrointestinal Haemorrhage**
D. F. CANTWELL. *Clinical Radiology* [*Clin. Radiol.*] **11**, 60–64, Jan., 1960. 7 figs., 17 refs.

Patients admitted to hospital with acute haematemesis or melaena have in the past generally not been subjected to a barium radiological examination, on the grounds that this might aggravate the patient's often precarious condition. However, if such an examination can be carried out in the ward with the minimum of disturbance, using a mobile x-ray unit, the argument against immediate radiography does not apply and the author has carried out such barium-meal examinations on 200 patients admitted to the General Infirmary at Leeds as acute emergencies during the years 1956 to 1958. The examination was usually performed within 12 to 24 hours of admission, and at a later date it was usually possible to confirm or otherwise the initial diagnosis after gastroscopy, surgery, or further radiography.

The tabulated results show that a correct diagnosis was made in 165 cases; of these, the findings were negative in 50 and positive in 114, these including duodenal ulcer, gastric ulcer, hiatus hernia, oesophageal varices, duodenal diverticulum, gastric carcinoma, stomal ulcer, and jejuno-gastric intussusception. The initial diagnosis was incorrect in 36 cases (18%), false positive findings being the cause in 12.

These results suggest that there is a useful place for early barium-meal radiography of patients admitted with haemorrhage and that the information gained may be of considerable help if emergency surgery has to be undertaken.

A. M. Rackow

829. **Investigations into the Value of Adding Sorbitol to the Barium Mixture for Examination of the Gastrointestinal Canal.** (Untersuchungen über den Wert einer Sorbitolbeimischung zum Bariumbrei für die Röntgendarstellung des Darmtraktes)
K. REINHARDT. *Fortschritte auf dem Gebiete der Röntgenstrahlen und der Nuklearmedizin* [*Fortschr. Röntgenstr.*] **92**, 78–84, Jan., 1960. 5 figs., 3 refs.

At the Hüttenkrankenhaus, Völklingen, 50 unselected patients were given a barium meal [? volume] containing 20 g. of sorbitol. In 60% of the cases "in which we made exposures after 45 minutes" the caecum was visualized, and after 3 hours the splenic flexure of the colon. In "16% of our cases" the whole intestinal tract was filled without large sections being left empty. Unfortunately it was impossible to anticipate the moment at which this would occur.

[No control series is described. In the abstracter's experience sorbitol has no advantage over other substances which delay water absorption in the small intestine.]

Denys Jennings

830. **Diagnostic Roentgenology of the Digestive Tract without Contrast Media.** [Monograph]
B. S. WOLF, M. T. KHILNANI, and A. LAUTKIN. *Journal of the Mount Sinai Hospital* [*J. Mt Sinai Hosp.*] **27**, 101–276, March–April, 1960. 245 figs., 43 refs.

831. **Reactions Associated with Intravenous Urography: Discussion of Mechanisms and Therapy**
E. A. HILDRETH, H. P. PENDERGRASS, R. L. TONDREAU, and D. J. RITCHIE. *Radiology* [*Radiology*] **74**, 246–254, Feb., 1960. 1 fig., 35 refs.

The incidence of fatal and nonfatal reactions to intravenous pyelography has risen during the last 3 years coincident with the increased use of this diagnostic

procedure. While the precise mechanism of the severe reactions is not known, there is a strong probability that they are allergic in origin. The authors have studied this problem, and in this paper they describe the routine for prophylaxis and treatment as carried out in the Department of Radiology, University of Pennsylvania, Philadelphia. Approximately 12 to 24 hours before the examination 0·1 to 0·2 ml. of the contrast material diluted 1:10 is injected subcutaneously as a test dose. At the time of the examination the first 1 ml. is injected and there is a pause of at least one minute before the remainder is given. If a reaction is suspected at least 5 minutes—and preferably 15 to 20 minutes—should elapse while 5% glucose is infused slowly through a three-way stopcock. After the actual injection the patient is kept under close observation for 15 to 30 minutes.

As regards treatment of a severe reaction, the authors emphasize the importance of acting immediately symptoms occur. Adrenaline is considered to be the drug of choice. Cortisone-like drugs are of no help in the first and most critical minutes, but are valuable for prolonged effects. *D. E. Fletcher*

832. **Pyelography in Renal Disease with Hypertension. Correlation between Pyelographic Findings and Differential Renal Function Studies**
L. F. Squire and J. U. Schlegel. *Radiology* [*Radiology*] 73, 849–864, Dec., 1959. 9 figs., 33 refs.

Hypertension in some cases is due to unilateral kidney disease and may be cured if the affected kidney is removed or repaired in time. The intravenous pyelogram may be misleading in that it reveals apparently normal kidneys in which concentration of the contrast medium appears equal on both sides. This does not necessarily imply that both kidneys are functioning normally, and differential function studies with catheters in both ureters may be employed as a means of assessment. Of value in this connection are the inulin clearance test and diodone or *para*-aminohippuric acid clearance test.

In this paper from the University of Rochester School of Medicine, New York, the findings in 17 patients with hypertension are discussed. In all except one of the patients excretion of the contrast medium was of good density on both sides, although biochemical tests indicated a unilateral or bilateral depression of function. Some abnormality indicating the affected side was seen in 8 of the intravenous pyelograms, but in 9 the findings were no index to the fact that unilateral kidney disease existed. Aortograms were obtained in 8 of the 17 cases and in 7 of these an abnormality on one side was demonstrated.

In 6 out of 8 patients operated on the blood pressure returned to normal; in the remaining 2 the long history of hypertension preceding the operation probably contraindicated nephrectomy and the blood pressure did not change. Among the lesions found in the 17 cases were anomalous arterial supply, renal artery aneurysm, contracted kidney possibly due to old infarction, depression of function probably due to past pyelonephritis, and renal atherosclerosis. *A. M. Rackow*

833. **The Radiological Lesions of Gout.** (Les lésions radiologiques de la goutte)
S. de Sèze, A. Ryckewaert, J. Levernieux, and R. Marteau. *Journal de radiologie, d'électrologie et de médecine nucléaire* [*J. Radiol. Électrol.*] **41**, 1–13, Jan.–Feb., 1960. 18 figs., 36 refs.

The authors have examined the joints of the hands and feet and any other involved joints in a series of 50 gouty patients with tophi and 50 without tophi, and here describe the incidence and nature of the radiological changes. Articular lesions included narrowing of the joint space, marginal osteophytes, and subarticular cysts, referred to as geodes or dilated lymph spaces. Notching of the articular surfaces often resulted from the development of a geode, but was sometimes caused by direct pressure from a tophus. Among the para-articular lesions seen radiologically were roughening of muscle attachments, not regarded as pathognomonic, and actual visualization of tophi as soft-tissue shadows which sometimes were partially calcified.

The incidence of bone changes was much higher among the patients with tophi, in whom also the lesions were more severe with a consequently poorer prognosis. A definite radiological diagnosis, however, could only be made in just under half the cases, and to a large extent it depended on the presence of geodes having a diameter of more than 5 mm. Severe lesions were not necessarily accompanied by severe signs or symptoms, but such joints had always been the site of symptoms at some former time. Osteoporosis was not a feature, except in a transient form associated with gouty crises.

The lesions in the foot followed a relatively constant pattern, particularly affecting the joints of the great toe and the fifth metatarso-phalangeal joint. In the hands, on the contrary, the areas of destruction were quite haphazard in distribution. The involvement of other joints was relatively unusual, but the authors call attention to changes conforming to this type occurring round the ankle and in the olecranon process of the ulna.
R. O. Murray

RADIOTHERAPY

834. **Total Thoracic Irradiation Combined with Intravenous Injection of Autogenous Marrow**
K. A. Newton. *Clinical Radiology* [*Clin. Radiol.*] **11**, 14–21, Jan., 1960. 8 figs., 11 refs.

In malignant conditions haematopoietic depression is one of the obstacles to the irradiation of large areas of the body and often results in treatment being discontinued before a lethal dose to the tumour has been given, this being particularly so when the thorax is irradiated. This paper from the Westminster Hospital, London, describes 7 cases in which total thoracic irradiation was carried out for widespread pulmonary metastases and was followed by an intravenous injection of autogenous marrow, the object being to repopulate the denuded bone-marrow spaces.

Of the 7 cases, in all but one of which there were pulmonary metastases from a radiosensitive primary tumour, 5 showed evidence of repopulation after reinfusion of the

marrow and 2 of these patients have survived for more than 4 months, apparently free from disease; in the other 3 patients there was complete disappearance of metastatic disease, but they later died from radiation pneumonitis. The remaining 2 patients died of uncontrollable malignant disease. Because of the problem of the appearance of radiation pneumonitis following a dosage of 3,000 r. or more given in 2 weeks the author reduced the dose rate to 150 r. daily and limited the total dose to 2,500 r. Both of the survivors mentioned above were in the latter group and accordingly the author recommends that 2,500 r. given at a rate of 150 r. daily should not be exceeded. Case histories are briefly described.

In most of these cases marrow was aspirated before the start of treatment and stored at −79° C. It was, however, shown that marrow aspirated after treatment from a non-irradiated area was also effective. An anaesthetic is necessary in aspirating the marrow. Chronic bronchitis and emphysema are regarded as a contraindication to total thoracic irradiation.

W. Constable

835. **The Effects of Radiation on the Lungs in the Treatment of Carcinoma of the Bronchus**

T. J. DEELEY. *Clinical Radiology* [*Clin. Radiol.*] **11**, 33–39, Jan., 1960. 12 figs., 4 refs.

This paper from the M.R.C. Radiotherapeutic Research Unit, Hammersmith Hospital, London, describes the radiological, physiological, and pathological changes occurring in the lungs following irradiation with the 8-MeV linear accelerator as seen in 61 patients with proved inoperable carcinoma of the bronchus; only patients surviving for at least one year after treatment were included in the study. All had received radical treatment, the mean total dose to the tumour being 4,500 rads in 4 weeks, except in some cases in which the field exceeded 200 sq. cm., when it was limited to 3,600 rads. As far as possible two non-opposed wedged fields were used so as to spare the spinal cord and opposite lung.

The radiological response was of two types: (1) in 27 (44%) of the patients there was an initial increase in size of the opacity occurring between 3 and 8 months after treatment, followed by subsequent reduction in its size as the result of fibrosis and shrinkage; (2) the remaining majority of cases, however, showed lung shrinkage without an initial increase in size of the opacity. In both groups emphysematous changes occurred in the unaffected lung coincidental with the fibrosis in the affected lung. Lung shrinkage develops rapidly after treatment; thus a graph shows that at 6 months there was some evidence of shrinkage in 90% of the cases, while this figure had increased to 95% at one year. In 23 patients who survived for 2 years or more such shrinkage was evident in all of them at 14 months.

Immediately after treatment there is usually palliation of most of the original symptoms, and some patients complain of no further symptoms, although they show radiological evidence of fibrosis. When symptoms occur they consist in cough and dyspnoea, and may variously be due to recurrence of the carcinoma, to the fibrosis, or to infection of the diseased lung; in some of the author's patients frequent attacks of infection occurred accompanied by increasing dyspnoea between the acute episodes, these attacks being attributed to infection of a lung already damaged by fibrosis. In one patient who died of cor pulmonale post-mortem examination revealed marked fibrosis at the site of the primary tumour, but no evidence of recurrence of the cancer. The results of pulmonary function tests, carried out on 28 patients and presented in a composite graph, show that there was a slight increase in vital capacity over the first 4 to 5 months, but thereafter it fell steadily until at the end of a year it was only about 75% of the value before treatment. The initial improvement is thought to be due to the effect of radiation on the tumour, whereas the subsequent fall is probably attributable to the fibrosis or to an increase in size of the tumour.

The pathology in the cases examined post mortem is described and the differential diagnosis of radiation effects in the normal lung is discussed. The value of the early use of antibiotics in the treatment of infections occurring in fibrosed lungs is stressed. In severe cases of fibrosis the possibility of performing pneumonectomy should be considered. Finally from a comparison of the amount of lung shrinkage in the present series with that in 27 similar patients treated with 240-kV. x rays the author concludes that there was no significant difference in the time interval or extent of shrinkage in the two groups.

K. S. Holmes

836. **Tumors of the Testis**

R. G. PARKER and J. B. HOLYOKE. *American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine* [*Amer. J. Roentgenol.*] **83**, 43–65, Jan., 1960. 16 figs., 23 refs.

The authors describe their experience in the treatment of 97 cases of tumour of the testis seen at the Swedish Hospital, Seattle, between 1940 and 1955. Classification by type of tumour was as follows: seminoma 49 cases, embryonal carcinoma 21, teratocarcinoma 19, choriocarcinoma 2, interstitial-cell tumour 3, and lymphoma 3; there were no cases of " pure " teratoma. Among the 21 tables presented, two show the relationship of survival to features such as volume of tumour, invasion of blood vessels, and degree of penetration of the tunica albuginea and epididymis. Details of the clinical features of each type are described and the authors draw attention to the poor prognosis which is associated with the finding of gynaecomastia.

In the discussion of treatment policy initial orchidectomy with thorough dissection of the inguinal canal is advocated. Retroperitoneal dissection is discarded in favour of radiation therapy to the abdominal lymph nodes to just above the renal pedicles, this being offered to all patients as a routine. Irradiation of the mediastinum and left supraclavicular fossa is given in addition when there is evidence of metastasis to these sites. Few complications of radiotherapy were observed owing to the comparatively small volumes irradiated and the avoidance of the major part of the renal parenchyma. The contralateral testis was not irradiated directly and 10 of the patients became fathers after treatment, there being

no recorded gross abnormalities in the children. Further tables given show the marked progress in treatment, especially of seminoma, after 1950 (when radiation planning and dosage techniques were improved) compared with earlier years at this hospital.

The authors quote their results in detail and conclude that the dose required to cure seminoma is of the order of 2,500 to 3,000 r. given over 4 weeks, but that 3,500 to 4,000 r. over 6 weeks is required for embryonal carcinoma. They also favour the view that a mature teratomatous component of the tumour, for example, teratocarcinoma, indicates a less malignant course.

I. D. H. Todd

837. **The Use of a Cobalt 60 Beam Unit for the Treatment of Carcinoma of the Larynx**

R. C. Tudway and H. F. Freundlich. *British Journal of Radiology* [*Brit. J. Radiol.*] **33**, 98–104, Feb., 1960. 3 figs., 4 refs.

The authors compare the results obtained at Bristol Royal Hospital in the treatment of carcinoma of the larynx in 65 patients seen between 1948 and 1953 and 62 seen between 1955 and 1958 after the introduction of radioactive cobalt (^{60}Co) therapy. Growths of the true cords (including subglottic tumours), the false cords, the vestibule, the arytenoids, the aryepiglottic folds, and the base of the epiglottis were treated, but not growths of the pyriform fossa.

Between 1948 and 1953 laryngectomy was carried out in early cases and x-irradiation in more advanced cases (about 60% of the total). Since 1953 treatment with ^{60}Co has been the method of choice and has been used in 80% of cases. Laryngectomy is now performed in only 8% of cases. In order to assess the results the authors make use of Boag's statistical method of forecasting 5-year results. This is worked out in detail with references to Boag's original paper (*Brit. J. Radiol.*, 1948, **21**, 128 and 189). The authors consider that with ^{60}Co therapy the over-all 5-year cure rate in carcinoma of the larynx may be raised from about 36% to over 50%.

E. Stanley Lee

838. **Rotational Cobalt 60 Teletherapy of Vesical Cancer**

H. H. Browne and R. T. Ogden. *American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine* [*Amer. J. Roentgenol.*] **83**, 107–115, Jan., 1960. 8 figs., 9 refs.

The authors report the results obtained by means of irradiation with radioactive cobalt (^{60}Co) teletherapy in the treatment of carcinoma of the urinary bladder at Hartford Hospital, Connecticut, from December, 1954, to January, 1958, and compare them with the results of surgery at the same hospital and elsewhere. The follow-up period ranged from one to 4 years. Of the 55 proved cases of carcinoma of the bladder treated, 47 were given the same type of therapy, receiving a dose of 5,000 to 6,000 r. in 5 to 6 weeks through fields of 10×10 or 10×15 cm. at the tumour depth centred over the bladder; 42 (90%) of the 47 cases were treated with complete rotation of the beam.

Of the 55 patients, there are 21 survivors, these including all (100%) of 10 patients who had Stage A-B disease, 5 (62%) of 8 patients with Stage-C disease, 4 (17%) of 23 with Stage-D disease, and 2 (14%) of 14 with inoperable disease. The only comparable figure available for patients treated surgically at the Hartford Hospital was a 72% survival rate for those with Stage A-B disease, all those with Stage C, D, and inoperable disease being dead. The results of irradiation of bladder cancer in all stages at this hospital were thus better than the surgical results. In addition 46 (83%) of the present 55 patients received useful palliation. Complications of a severe nature occurred in 5 cases (9%), 3 of these developing a haemorrhagic cystitis and 2 post-irradiation changes in the bowel. Comparison is also made with the preliminary results of radical cystectomy and pelvic exenteration reported by Whitmore and Marshall (*Surg. Clin. N. Amer.*, 1953, **33**, 501), who reported a survival rate of 72% in patients with disease in Stage A-B, a rate very close to the 71%, mentioned above, among such patients treated surgically.

R. S. Pointon

839. **Treatment of Papillomata of the Bladder with Radioactive Colloidal Gold (Au^{198})**

R. J. Dickson and E. K. Lang. *American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine* [*Amer. J. Roentgenol.*] **83**, 116–122, Jan., 1960. 3 figs., 20 refs.

The authors report, from Johns Hopkins Hospital, Baltimore, their 3 years' experience in the treatment of papillomatosis of the urinary bladder with radioactive colloidal gold (^{198}Au). The gold solution was introduced through a Foley catheter directly into the bladder, the capacity of which had been previously estimated by means of cystoscopy and cystometry, and left *in situ* for an "average" time of 2 to 3 hours. The dosage delivered to the bladder mucosa was calculated from a nomogram based upon the mean volume of the solution in the bladder, the dose aimed at being 6,000 r.e.p. in two applications. Of 21 patients in whom treatment was complete more than 6 months before this report, 17 had disease in Stage O; of these, 14 showed encouraging results. In patients with more infiltrative lesions, however, there was little benefit from the treatment. The most frequent complications were cystitis and anterior urethritis.

The authors state that the principal disadvantages of the method are: (1) the difficulty in assessing the degree of infiltration of the tumour in all areas of the bladder; (2) the recurrence of papillomata at the vesical neck in an area which is shielded from the colloidal solution by the bag of the Foley catheter; (3) the risk that some of the gold may remain outside the bladder in the infusion apparatus unless great care is taken; and (4) that the complications of treatment are not inconsiderable. These complications appeared to occur more commonly when treatment followed immediately after a surgical procedure, and the authors now recommend that the reaction following fulguration should be allowed to subside before treatment with ^{198}Au is attempted.

R. S. Pointon

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